UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 10-K

(Mark One)

☒ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the fiscal year ended December 31, 2022

or

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the transition period from to

Commission File No. 000-30319

INNOVIVA, INC.
(Exact name of registrant as specified in its charter)

Delaware (State or other jurisdiction of incorporation or organization)	**94-3265960** (I.R.S. Employer Identification No.)
1350 Old Bayshore Highway, Suite 400 **Burlingame, CA** (Address of principal executive offices)	**94010** (Zip Code)

Registrant's telephone number, including area code: **(650) 238-9600**

Title of Each Class	**Trading Symbol(s)**	**Name of Each Exchange On Which Registered**
Common Stock $0.01 Par Value	INVA	The Nasdaq Stock Market LLC

SECURITIES REGISTERED PURSUANT TO SECTION 12(g) OF THE ACT: **NONE**

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes ☒ No ☐

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. Yes ☐ No ☒

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes ☒ No ☐

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§ 232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). Yes ☒ No ☐

Indicate by check mark whether registrant is a large accelerated filer, an accelerated filer or a non-accelerated filer. See definition of "accelerated filer and large accelerated filer" in Rule 12b-2 of the Exchange Act (Check One):

Large accelerated filer ☒ Accelerated filer ☐ Non-accelerated filer ☐ Smaller reporting company ☐
Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Indicate by check mark whether the registrant has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report. ☒

If securities are registered pursuant to Section 12(b) of the Act, indicate by check mark whether the financial statements of the registrant included in the filing reflect the correction of an error to previously issued financial statements. ☐

Indicate by check mark whether any of those error corrections are restatements that required a recovery analysis of incentive-based compensation received by any of the registrant's executive officers during the relevant recovery period pursuant to §240.10D-1(b). ☐

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes ☐ No ☒

The aggregate market value of the voting and non-voting common equity held by non-affiliates of the registrant based upon the closing price of the registrant's Common Stock on The Nasdaq Global Select Market on June 30, 2022 was $923,930,805. This calculation does not reflect a determination that persons are affiliates for any other purpose.

On February 14, 2023, there were 68,126,089 shares of the registrant's Common Stock outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Specified portions of the registrant's definitive Proxy Statement to be issued in conjunction with the registrant's 2023 Annual Meeting of Stockholders, which is expected to be filed not later than 120 days after the registrant's fiscal year ended December 31, 2022, are incorporated by reference into Part III of this Annual Report. Except as expressly incorporated by reference, the registrant's Proxy Statement shall not be deemed to be a part of this Annual Report on Form 10-K.

INNOVIVA, INC.
2022 Form 10-K Annual Report

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Special Note Regarding Forward-Looking Statements

This Annual Report on Form 10-K contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended (the "Securities Act"). Such forward-looking statements involve substantial risks, uncertainties and assumptions. All statements in this Annual Report on Form 10-K, other than statements of historical fact, including, without limitation, statements regarding our strategy, future operations, future financial position, future revenue, projected costs, prospects, plans, intentions, expectations, goals and objectives may be forward-looking statements. The words "anticipates," "believes," "could," "designed," "estimates," "expects," "goal," "intends," "may," "objective," "plans," "projects," "pursuing," "will," "would" and similar expressions (including the negatives thereof) are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. We may not actually achieve the plans, intentions, expectations or objectives disclosed in our forward-looking statements and the assumptions underlying our forward-looking statements may prove incorrect. Therefore, you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions, expectations and objectives disclosed in the forward-looking statements that we make. All written and verbal forward-looking statements attributable to us or any person acting on our behalf are expressly qualified in their entirety by the cautionary statements contained or referred to in this section.

Important factors that we believe could cause actual results or events to differ materially from our forward-looking statements include, but are not limited to, risks related to: lower than expected future royalty revenue from respiratory products partnered with GSK, the commercialization of RELVAR®/BREO® ELLIPTA®, ANORO® ELLIPTA®, GIAPREZA® and XERAVA® in the jurisdictions in which these products have been approved; the strategies, plans and objectives of the Company (including the Company's growth strategy and corporate development initiatives); the timing, manner, and amount of potential capital returns to shareholders; the status and timing of clinical studies, data analysis and communication of results; the potential benefits and mechanisms of action of product candidates; expectations for product candidates through development and commercialization; the timing of regulatory approval of product candidates; and projections of revenue, expenses and other financial items; the impact of the novel coronavirus ("COVID-19"); the timing, manner and amount of capital deployment, including potential capital returns to stockholders; and risks related to the Company's growth strategy and risks discussed in "Risk Factors" in Item 1A of Part I, "Management's Discussion and Analysis of Financial Condition and Results of Operations" in Item 7 of Part II and elsewhere in this Annual Report on Form 10-K. Our forward-looking statements in this Annual Report on Form 10-K are based on current expectations as of the date hereof and we do not assume any obligation to update any forward-looking statements on account of new information, future events or otherwise, except as required by law.

We encourage you to read Management's Discussion and Analysis of our Financial Condition and Results of Operations and our consolidated financial statements contained in this Annual Report on Form 10-K. We also encourage you to read Item 1A of Part I of this Annual Report on Form 10-K, entitled "Risk Factors," which contains a more complete discussion of the risks and uncertainties associated with our business. In addition to the risks described above and in Item 1A of this report, other unknown or unpredictable factors also could affect our results. Therefore, the information in this report should be read together with other reports and documents that we file with the Securities and Exchange Commission ("SEC") from time to time, including on Form 10-Q and Form 8-K, which may supplement, modify, supersede or update those risk factors. As a result of these factors, we cannot assure you that the forward-looking statements in this report will prove to be accurate. Furthermore, if our forward-looking statements prove to be inaccurate, the inaccuracy may be material. In light of the significant uncertainties in these forward-looking statements, you should not regard these statements as a representation or warranty by us or any other person that we will achieve our objectives and plans in any specified time frame, or at all.

PART I

ITEM 1. BUSINESS

Overview

Innoviva, Inc. ("Innoviva", the "Company", the "Registrant" or "we" and other similar pronouns) is a diversified holding company with a portfolio of royalties and other healthcare assets. Our royalty portfolio contains respiratory assets partnered with Glaxo Group Limited ("GSK"), including RELVAR®/BREO® ELLIPTA® (fluticasone furoate/vilanterol, "FF/VI") and ANORO® ELLIPTA® (umeclidinium bromide/vilanterol, "UMEC/VI"). Under the Long-Acting Beta2 Agonist ("LABA") Collaboration Agreement, Innoviva is entitled to receive royalties from GSK on sales of RELVAR®/BREO® ELLIPTA® as follows: 15% on the first $3.0 billion of annual global net sales and 5% for all annual global net sales above $3.0 billion; and royalties from the sales of ANORO® ELLIPTA®, which tier upward at a range from 6.5% to 10%. Innoviva was also entitled to 15% of royalty payments made by GSK under its agreements originally entered into with us, and since assigned to Theravance Respiratory Company, LLC ("TRC"), including TRELEGY® ELLIPTA® and any other product or combination of products that may be discovered or developed in the future under the LABA Collaboration Agreement and the Strategic Alliance Agreement with GSK (referred to herein as the "GSK Agreements"), which were assigned to TRC other than RELVAR®/BREO® ELLIPTA® and ANORO® ELLIPTA®. We sold our 15% ownership interest in TRC on July 20, 2022, and are no longer entitled to receive royalties on sales of TRELEGY® ELLIPTA® products.

We expanded our portfolio of royalties and innovative healthcare assets through the acquisition of Entasis Therapeutics Holdings Inc. ("Entasis") on July 11, 2022 and the acquisition of La Jolla Pharmaceutical Company ("La Jolla") on August 22, 2022. Our commercial and marketed products include GIAPREZA® (angiotensin II), approved in the United States ("U.S.") to increase blood pressure in adults with septic or other distributive shock, and XERAVA® (eravacycline) approved in the U.S. for the treatment of complicated intra-abdominal infections in adults. Our development pipeline includes medicines for the treatment of bacterial infections, such as our lead asset sulbactam-durlobactam ("SUL-DUR").

Our headquarters are located at 1350 Old Bayshore Highway, Suite 400, Burlingame, CA 94010. The Company was incorporated in Delaware in November 1996 under the name Advanced Medicine, Inc., and began operations in May 1997. It later changed its name to Theravance, Inc. in April 2002. In June 2014, we spun-off our research and development operations. In January 2016, we rebranded and changed our name to Innoviva, Inc.

Our Strategy

Our corporate strategy is currently focused on increasing stockholder value by, among other things, maximizing the potential value of our respiratory assets partnered with GSK, optimizing our operations and augmenting capital allocation. We continue to diversify our royalty management business through actively pursuing opportunistic acquisitions of promising companies and assets in the healthcare industry and enhancing the returns on our capital. In particular, our recent acquisitions of Entasis and La Jolla created a robust hospital and infectious disease platform.

Our Royalty Product Portfolio

Our Relationship with GSK

LABA Collaboration

In November 2002, we entered into our LABA Collaboration Agreement with GSK to develop and commercialize once-daily products for the treatment of chronic obstructive pulmonary disease ("COPD") and asthma. The collaboration has developed three combination products, two of which we still retain rights in. Those two are as follows:

- RELVAR®/BREO® ELLIPTA® ("FF/VI") (BREO® ELLIPTA® is the proprietary name in the U.S. and Canada and RELVAR® ELLIPTA® is the proprietary name outside the U.S. and Canada), a once-daily combination medicine consisting of a LABA, vilanterol ("VI"), and an inhaled corticosteroid ("ICS"), fluticasone furoate ("FF"), and,

- ANORO® ELLIPTA® ("UMEC/VI"), a once-daily medicine combining a long-acting muscarinic antagonist ("LAMA"), umeclidinium bromide ("UMEC"), with a LABA, VI.

As a result of the launch and approval of RELVAR®/BREO® ELLIPTA® and ANORO® ELLIPTA® in the U.S., Japan and Europe, in accordance with the LABA Collaboration Agreement, we paid milestone fees to GSK totaling $220.0 million during the year ended December 31, 2014. The milestone fees paid to GSK were recognized as capitalized fees paid, which are being amortized over their estimated useful lives commencing upon the commercial launch of the products.

Competition

We anticipate that RELVAR®/BREO® ELLIPTA® (FF/VI) and ANORO® ELLIPTA® (UMEC/VI) will compete with a number of approved bronchodilator drugs alone or in combination, including each other and drug candidates under development that are designed to treat asthma and COPD. These include but are not limited to:

- Advair®/Seretide™ Diskus®/HFA® (salmeterol and fluticasone propionate as a combination) marketed by GSK
- Symbicort® (formoterol and budesonide as a combination) marketed by AstraZeneca
- AirDuo Respiclick® (salmeterol and fluticasone propionate), a non-substitutable generic version of Advair, marketed by TEVA
- Spiriva® Handihaler® and Spiriva® Respimat® (tiotropium) marketed by Boehringer Ingelheim
- Dulera® (formoterol and mometasone as a combination) marketed by Merck
- Tudorza® Pressair® (aclidinium) marketed by AstraZeneca and Seebri® Breezehaler® (glycopyrronium) marketed by Novartis outside the U.S. and Sunovion in the U.S.
- Incruse® Ellipta® (umeclidinium) and Arnuity® Ellipta® (fluticasone furoate) (Innoviva is not entitled to any royalties from either product)
- Foradil® Aerolizer®/Oxis® Turbuhaler® (formoterol) marketed by a number of companies
- Striverdi® Respimat® (olodaterol) marketed by Boehringer Ingelheim
- Onbrez® Breezehaler® (E.U.)/Arcapta® Neohaler® (U.S.) (indacaterol) marketed by Novartis
- Ultibro® Breezehaler® (E.U.)/Utibron® Neohaler® (U.S.) (indacaterol combined with glycopyrronium bromide) developed by Novartis and approved and launched in Europe and Japan in the year ended December 31, 2013 as a once-daily treatment for COPD. In the U.S., the product was approved in October 2015 at a lower strength as a twice-daily COPD treatment, and was licensed to Sunovion in December 2016, and launched in May 2017
- Stiolto (U.S.)/Spiolto (E.U.) Respimat® (tiotropium combined with olodaterol) marketed by Boehringer Ingelheim for the treatment of COPD
- Bevespi Aerosphere® (glycopyrronium bromide in combination with formoterol fumarate) marketed by AstraZeneca
- Duaklir® Genuair® (aclidinium bromide in combination with formoterol fumarate) developed by AstraZeneca as a maintenance bronchodilator treatment for COPD and approved in November 2014 in the EU and March 2019 in the U.S.
- QMF149 (indacaterol in combination with mometasone) developed by Novartis for markets outside the U.S. and under regulatory review in the E.U. for asthma. In Phase 3 development for COPD
- Trimbow (a fixed-dose, twice daily combination of formoterol, beclomethasone and glycopyrronium) manufactured by Chiesi and indicated for use in COPD in the E.U.
- Foster (beclomethasone dipropionate in combination with formoterol fumarate) manufactured by Chiesi and indicated for use in asthma and COPD outside the U.S.
- Enerzair Breezehaler (QVM149) (a fixed-dose combination of indacaterol, mometasone and glycopyrronium) developed by Novartis as a triple therapy/single inhaler for the treatment of asthma and approved in the E.U., Canada, and Japan

- Breztri Aerosphere (fixed dose combination of formoterol, glycopyrronium and budesonide) developed by AstraZeneca as a triple therapy single inhaler twice-daily medication for COPD and approved in the U.S. in July 2020
- Nucala (mepolizumab; an interleukin-5 antagonist monoclonal antibody) developed by GSK for add on maintenance treatment of severe asthma in patients 12 years and older and approved in the U.S. in June 2019
- Xolair® (omalizumab, an anti-IgE antibody) developed by Genentech for patients 6 years of age and older with moderate to severe persistent asthma uncontrolled by inhaled corticosteroids and approved in 2003. Single-dose pre-filled syringes were approved by the FDA in September 2018
- Cinqair® (anti-interleukin-5 monoclonal antibody for the add-on maintenance treatment of adults with severe asthma and an eosinophilic phenotype) marketed by TEVA Pharmaceutical Industries Ltd.
- Dupixent® (dupilamab, an injectable IL-4 and IL-13 inhibitor) developed by Sanofi Genzyme and approved by the FDA in October 2018 as an add-on maintenance therapy in patients with moderate-to-severe asthma aged 12 years and older with an eosinophilic phenotype or with oral corticosteroid-dependent asthma
- Fasenra® (benralizumab, an injectable anti-IL-5 monoclonal antibody) for the treatment of severe asthma in patients 12 years of age and older marketed by AstraZeneca. Fasenra Pen pre-filled auto-injector was approved by the FDA for self-administration in November 2019
- Singulair® (monteleukast), an orally active leukotriene receptor antagonist for the prophylaxis and treatment of asthma in patients 12 months of age and older marketed by Merck
- Tezspire® (tezepelumab-ekko), an injectable monoclonal antibody designed to inhibit thymic stromal lymphopoietin (TSLP), an epithelial cytokine thought to be critical in the initiation and persistence of airway inflammation. Co-developed by Astra Zeneca and Amgen for the treatment of severe asthma. The FDA approved the Tezspire solution for subcutaneous injection in December 2021; it is indicated for the add-on maintenance treatment of adult and pediatric patients aged 12 years and older with severe asthma.

In addition, several firms have been developing new formulations of Advair/Seretide (salmeterol /fluticasone propionate) and Symbicort (formoterol fumerate/budesonide) which may be marketed as generics or branded generics relative to the existing products from GSK and AstraZeneca, respectively. All of these efforts represent potential competition for any of our partnered products. Efforts have intensified following the publication of FDA draft guidance for the approval of fully substitutable versions of Advair and Symbicort in late 2013 and mid-2015, respectively. Current examples of these products include the marketed products Duoresp/Biresp from Teva (generic Symbicort), AirFluSal Forspiro by Sandoz, Rolenium by Elpen and Sirdupla by Mylan (all generic versions of Seretide) which are all available in a wide number of countries in the E.U. Numerous companies have brought to market generic forms of the ICS/LABA drug Advair® since certain patents covering the Advair® delivery device expired in 2016. In March 2017, Mylan N.V. received a complete response letter from the FDA relating to its Abbreviated New Drug Application ("ANDA") for fluticasone propionate 100, 250, 500 mcg and salmeterol 50 mcg inhalation powder. In May 2017, Hikma announced that it received a complete response letter from the FDA relating to its ANDA for fluticasone propionate and salmeterol inhalation powder, and in February 2018, Novartis announced that its generic division Sandoz had received a complete response letter from the FDA in response to its ANDA for a third fluticasone propionate and salmeterol product. In January 2019, Mylan announced that the FDA approved Wixela™ Inhu™ (fluticasone propionate and salmeterol inhalation powder, USP), the first generic of Advair Diskus® and Sandoz terminated development of generic Advair. Teva announced that the FDA approved two of its products for adolescent and adult patients with asthma, one of which is AirDuo™ RespiClick® (fluticasone propionate and salmeterol inhalation powder), a non-AB substitutable generic version of Advair®. In May 2020, Cipla filed for FDA approval of a generic version of Advair®. In April 2021, Hikma launched a generic version of Advair Diskus® in the U.S. In January 2020, Astra Zeneca launched an authorized generic version of Symbicort. In August 2021, Lupin launched Luforbec®, a branded generic alternative to Foster, in select European markets.

In general, these manufacturers are required to conduct a number of clinical efficacy, pharmacokinetic and device studies to demonstrate equivalence to Advair, per the FDA's September 2013 Draft Guidance Document. These studies are designed to demonstrate that the generic product has the same active ingredient(s), dosage form, strength, exposure and clinical efficacy as the branded product. These generic equivalents, which must meet the same exacting quality standards as branded products, may be significantly less costly to bring to market, and companies that produce generic equivalents are generally able to offer their products at lower prices. Thus, after the introduction of a generic competitor, a significant percentage of the sales of any branded product and products that may compete with such branded product is typically lost to the generic product. In addition, in April 2016, the FDA issued a draft guidance document covering Fluticasone Furoate/Vilanterol Trifenatate (FF/VI), the active ingredients used in RELVAR®/BREO® ELLIPTA®.

Our Integrated Hospital / Infectious Disease Business

Commercial and Marketed Products

The following table summarizes our commercial and marketed products:

Product	Indication	Pivotal Studies[1]	Regulatory Status
GIAPREZA® (angiotensin II)	Septic or other distributive shock[2]	321-patient, multinational, double-blind, randomized, placebo-controlled study	FDA-approved Dec 2017 European Commission-approved Aug 2019 NDA submitted in Great Britain (post-Brexit) Jan 2021
XERAVA® (eravacycline)	Complicated intra-abdominal infections[3],[4],[5]	538-patient, multinational, double-blind, randomized, active-controlled study 499-patient, multinational, double-blind, randomized, active-controlled study	FDA-approved Aug 2018 European Commission-approved Sep 2018 Singapore-approved Apr 2020 NDA submitted in Great Britain (post-Brexit) Jan 2021 NDA submitted in China Mar 2021 NDA submitted in Taiwan Aug 2022 Hong Kong-approved Sep 2022

(1) For U.S. and European approval
(2) U.S.: GIAPREZA is a vasoconstrictor to increase blood pressure in adults with septic or other distributive shock
(3) European Union: GIAPREZA is indicated for the treatment of refractory hypotension in adults with septic or other distributive shock who remain hypotensive despite adequate volume restitution and application of catecholamines and other available vasopressor therapies
(4) U.S.: XERAVA is a tetracycline class antibacterial indicated for the treatment of complicated intra-abdominal infections ("cIAI") in patients 18 years of age and older
(5) European Union: XERAVA is indicated for the treatment of cIAI in adults

GIAPREZA® (angiotensin II)

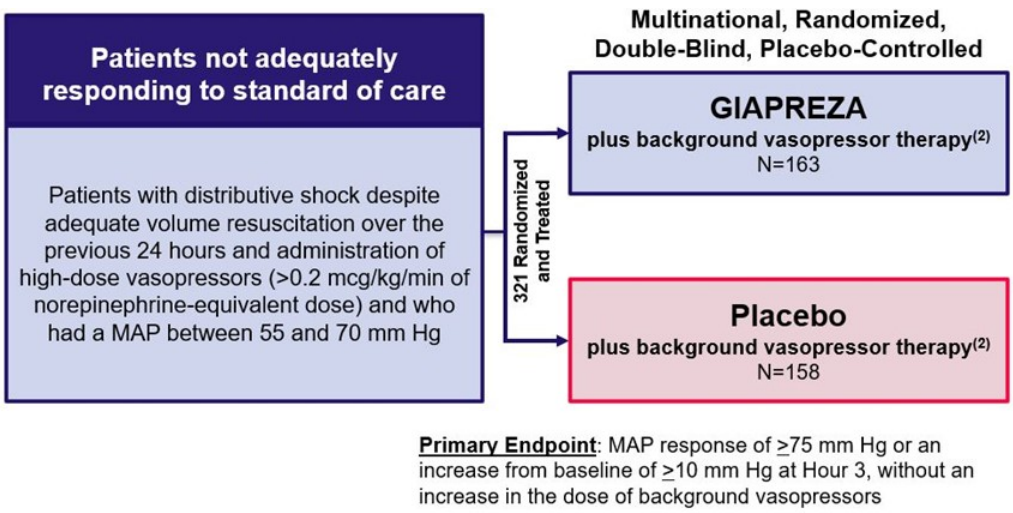
GIAPREZA® (angiotensin II) injection is approved by the U.S. FDA as a vasoconstrictor indicated to increase blood pressure in adults with septic or other distributive shock. GIAPREZA is approved by the European Commission ("EC") and by the Great Britain Medicines and Health Care Products Regulatory Agency ("MHRA") for the treatment of refractory hypotension in adults with septic or other distributive shock who remain hypotensive despite adequate volume restitution and application of catecholamines and other available vasopressor therapies. GIAPREZA mimics the body's endogenous angiotensin II peptide, which is central to the renin-angiotensin-aldosterone system ("RAAS"), which in turn regulates blood pressure. GIAPREZA is marketed in the U.S. by La Jolla and is marketed in Europe and Great Britain by PAION Deutschland GmbH ("PAION") on behalf of La Jolla.

Angiotensin II for the Treatment of High-Output Shock ("ATHOS-3")

GIAPREZA was approved by the U.S. FDA, EC and MHRA based on the results of ATHOS-3, which were published in the New England Journal of Medicine in August 2017. ATHOS-3 was a multinational, randomized, double-blind, placebo-controlled study in which 321 adults with septic or other distributive shock who remained hypotensive despite fluid and vasopressor therapy received either GIAPREZA or placebo, both in addition to background vasopressor therapy. The primary endpoint was mean arterial pressure

("MAP") response, defined as a MAP of 75 mm Hg or higher or an increase in MAP from baseline of at least 10 mm Hg without an increase in the dose of background vasopressors at Hour 3 (Khanna et al, New England Journal of Medicine 2017; 377:419–430).

ATHOS-3 Study Design[1]



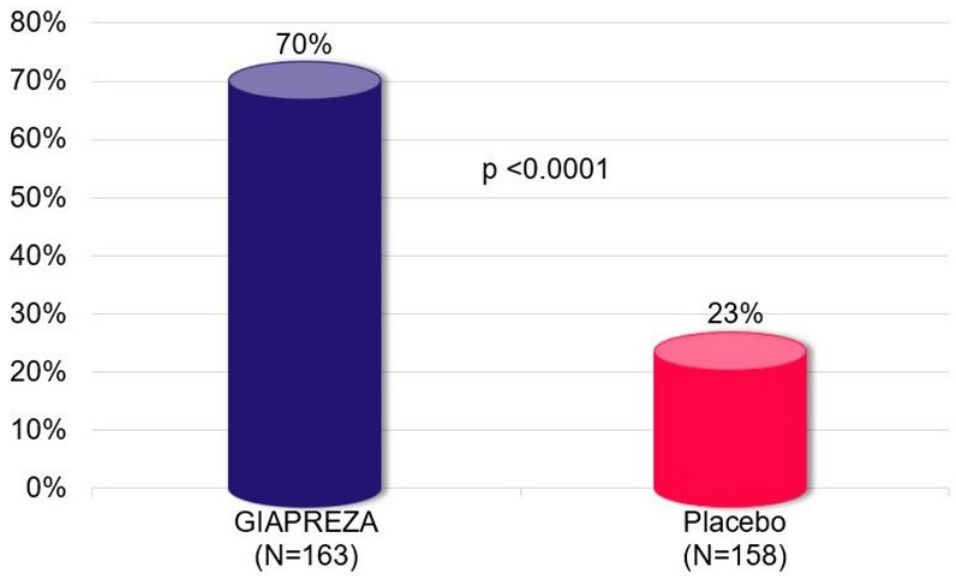
MAP=mean arterial pressure

(1) Khanna et al, New England Journal of Medicine 2017; 377:419–430

(2) Standard-of-care vasopressors included norepinephrine, epinephrine, dopamine and vasopressin

GIAPREZA significantly improved blood pressure response. Specifically, the primary endpoint was achieved by 70% of GIAPREZA-treated patients compared to 23% of placebo-treated patients (p <0.0001).

Primary Endpoint: Mean Arterial Pressure Response[1],[2]



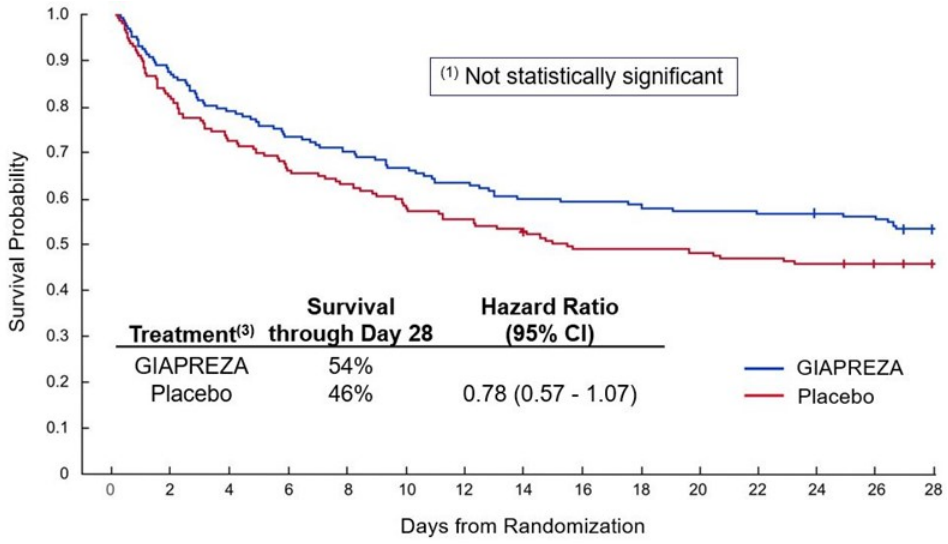
(1) GIAPREZA FDA prescribing information

(2) MAP response of 75 mm Hg or higher or an increase from baseline of at least 10 mm Hg at Hour 3 without an increase in the dose of background vasopressors

GIAPREZA provides the ability to rapidly achieve and adjust therapeutic response. GIAPREZA rapidly increased MAP with a median time to MAP response of approximately 5 minutes. The plasma half-life of GIAPREZA is less than 1 minute.

In addition, a positive survival trend was observed. Mortality through Day 28 was 46% on GIAPREZA and 54% on placebo (hazard ratio 0.78; 95% confidence interval 0.57–1.07).

Positive Survival Trend Observed (N=321)[1],[2]



(1) GIAPREZA FDA prescribing information

(2) MAP response of 75 mm Hg or higher or an increase from baseline of at least 10 mm Hg at Hour 3 without an increase in the dose of background vasopressors

The most common adverse reactions that were reported in greater than 10% of GIAPREZA-treated patients were thromboembolic events.

Adverse Reactions Occurring in ≥4% of Patients Treated with GIAPREZA and ≥1.5% More Often than in Placebo-treated Patients[1]

	GIAPREZA (N=163)	Placebo (N=158)
Thromboembolic events[2]	21 (12.9%)	8 (5.1%)
Deep vein thrombosis	7 (4.3%)	0 (0.0%)
Thrombocytopenia	16 (9.8%)	11 (7.0%)
Tachycardia	14 (8.6%)	9 (5.7%)
Fungal infection	10 (6.1%)	2 (1.3%)
Delirium	9 (5.5%)	1 (0.6%)
Acidosis	9 (5.5%)	1 (0.6%)
Hyperglycemia	7 (4.3%)	4 (2.5%)
Peripheral ischemia	7 (4.3%)	4 (2.5%)

(1) GIAPREZA FDA prescribing information
(2) Including arterial and venous thrombotic events

Percentage of Patients Experiencing ≥1 Adverse Event, ≥1 Serious Adverse Event and Discontinuing Treatment Due to an Adverse Event[1]

	GIAPREZA (N=163)	Placebo (N=158)
Percentage of patients experiencing ≥1 adverse event	87%	92%
Percentage of patients experiencing ≥1 serious adverse event	61%	67%
Percentage of patients discontinuing treatment due to an adverse event	14%	22%

(1) Khanna et al, *New England Journal of Medicine* 2017; 377:419–43

XERAVA® (eravacycline)

XERAVA® (eravacycline) for injection is approved by the U.S. FDA and Singapore Health Sciences Authority ("HSA") as a tetracycline class antibacterial indicated for the treatment of cIAI due to susceptible microorganisms in patients 18 years of age and older. XERAVA is approved by the EC, MHRA, and the Hong Kong Department of Health ("DoH") for the treatment of cIAI in adults. XERAVA is marketed in the U.S. by our wholly owned subsidiary, Tetraphase Pharmaceuticals, Inc. ("Tetraphase"), and is marketed in Europe and Great Britain by PAION on behalf of Tetraphase and is marketed in mainland China, Taiwan, Hong Kong, Macau, South Korea, Singapore, the Malaysian Federation, the Kingdom of Thailand, the Republic of Indonesia, the Socialist Republic of Vietnam and the Republic of the Philippines by Everest Medicines Limited ("Everest"). Everest submitted an NDA in China, which was accepted by the China National Medical Products Administration ("NMPA") in March 2021.

cIAIs are the second most common source of severe sepsis in the ICU (Brun-Buisson et al, JAMA 1995; 274(12):968–974). cIAIs are defined as consequences of perforations of the gastrointestinal tract that result in contamination of the peritoneal space (Solomkin et al, Clinical Infectious Diseases 2018; 69(6):921–929).

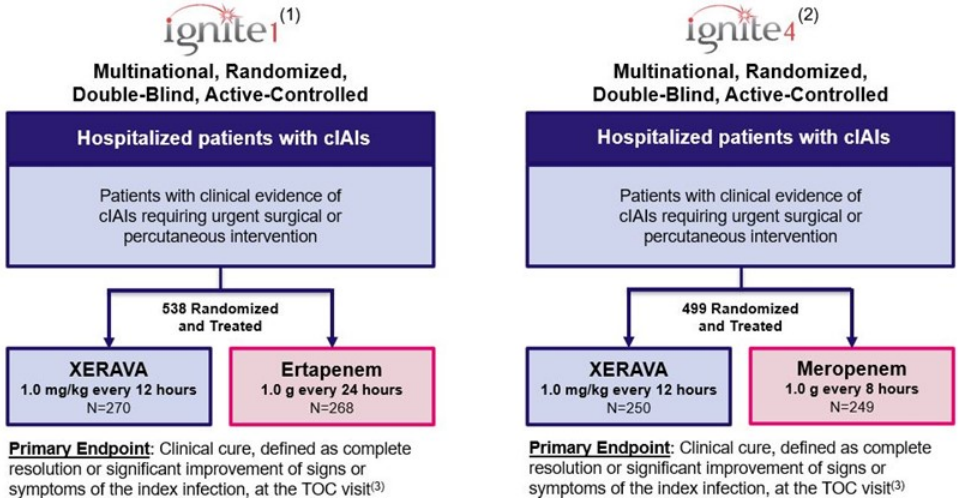
Investigating Gram-negative Infections Treated with Eravacycline ("IGNITE")

XERAVA was approved by the U.S. FDA, HSA, EC, MHRA, and DoH based on the results of IGNITE1 and IGNITE4, which were published in JAMA Surgery in March 2017 and Clinical Infectious Diseases in December 2018, respectively.

IGNITE1 was a multinational, randomized, double-blind, active-controlled study in 538 patients with clinical evidence of cIAIs requiring urgent surgical or percutaneous intervention who received either XERAVA or ertapenem. The primary endpoint was clinical cure, defined as complete resolution or significant improvement of signs or symptoms of the index infection, at the test of cure ("TOC") visit. The TOC visit was conducted 25 to 31 calendar days after the first dose of the study drug was administered.

IGNITE4 was a multinational, randomized, double-blind, active controlled study in 499 patients with clinical evidence of cIAIs requiring urgent surgical or percutaneous intervention who received either XERAVA or meropenem. The primary endpoint was clinical cure, defined as complete resolution or significant improvement of signs or symptoms of the index infection, at the TOC visit. The TOC visit was conducted 25 to 31 calendar days after the first dose of the study drug was administered.

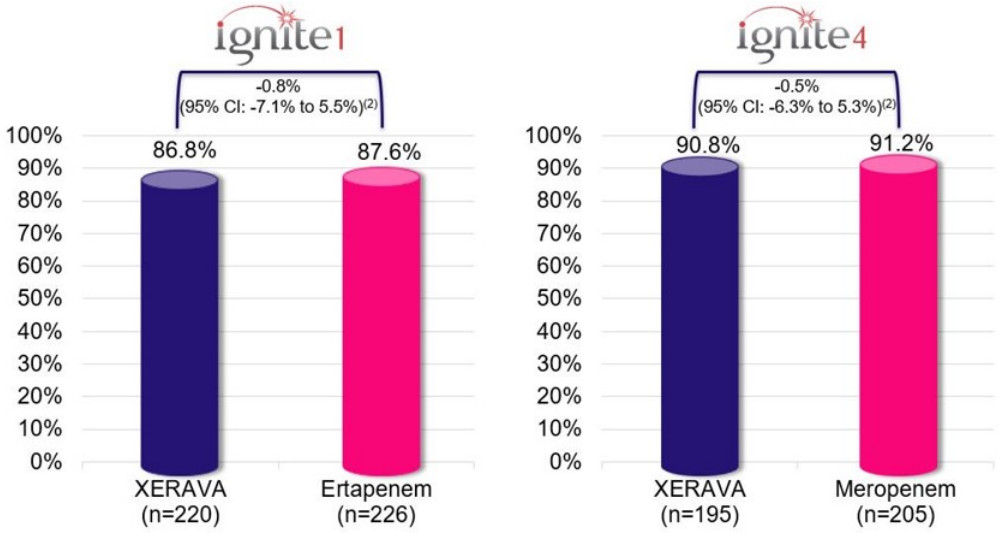
IGNITE1 and IGNITE4 Study Design



(1) Solomkin et al, *JAMA Surgery* 2017; 152(3):224-232
(2) Solomkin et al, *Clinical Infectious Diseases* 2018; 69(6):921-9
(3) TOC visit was conducted 25 to 31 calendar days after the first dose of the study drug was administered

XERAVA demonstrated statistical noninferiority in clinical cure rate in the micro-ITT population, which included all randomized subjects who had baseline bacterial pathogens that caused cIAIs and against at least one of which the investigational drug has in vitro (in a test tube) antibacterial activity (N=846).

Primary Endpoint: Clinical Cure Rate[1]



(1) XERAVA FDA prescribing information
(2) Noninferiority margins of 10% and 12.5% were used for IGNITE1 and IGNITE4, respectively

Clinical cure rates across patients with gram-negative, gram-positive and anaerobic pathogens, including those with resistant strains, are shown in the following tables.

Clinical Cure Rates at TOC by Selected Baseline Pathogens in the Micro-ITT Population[1]

	XERAVA N=415 n/N1	Comparators[2] N=431 n/N1
Enterobacteriaceae	271/314 (86.3%)	289/325 (88.9%)
Citrobacter freundii	19/22 (86.4%)	8/10 (80.0%)
Enterobacter cloacae complex	17/21 (81.0%)	23/24 (95.8%)
Escherichia coli	220/253 (87.0%)	237/266 (89.1%)
Klebsiella oxytoca	14/15 (93.3%)	16/19 (84.2%)
Klebsiella pneumoniae	37/39 (94.9%)	42/50 (84.0%)
Enterococcus faecalis	45/54 (83.3%)	47/54 (87.0%)
Enterococcus faecium	38/45 (84.4%)	48/53 (90.6%)
Staphylococcus aureus	24/24 (100.0%)	12/14 (85.7%)
Streptococcus anginosus group[3]	79/92 (85.9%)	50/59 (84.7%)
Anaerobes[4]	186/215 (86.5%)	194/214 (90.7%)

N=Number of subjects in the micro-ITT Population; N1=Number of subjects with a specific pathogen; n=Number of subjects with a clinical cure at the TOC visit
(1) XERAVA FDA prescribing information
(2) Comparators included ertapenem and meropenem for IGNITE1 and IGNITE4, respectively
(3) Includes *Streptococcus anginosus, Streptococcus constellatus, and Streptococcus intermedius*
(4) Includes *Bacteroides caccae, Bacteroides fragilis, Bacteroides ovatus, Bacteroides thetaiotaomicron, Bacteroides uniformis, Bacteroides vulgatus, Clostridium perfringens, and Parabacteroides distasonis*

XERAVA Demonstrated High Clinical Cure Rates Against Resistant Pathogens[1]

	XERAVA N=415 n/N1	Comparators[2] N=431 n/N1
Enterobacteriaceae	271/314 (86.3%)	289/325 (88.9%)
CEPH-R	43/48 (89.6%)	40/45 (88.9%)
ESBL confirmed	32/36 (88.9%)	25/29 (86.2%)
Carbapenemase[3]	1/1 (100.0%)	2/3 (66.7%)
MDR	40/46 (87.0%)	29/32 (90.6%)
Acinetobacter baumannii	13/13 (100.0%)	7/7 (100.0%)
CEPH-R	13/13 (100.0%)	5/5 (100.0%)
ESBL confirmed	5/5 (100.0%)	1/1 (100.0%)
Carbapenemase[3]	2/2 (100.0%)	4/4 (100.0%)
MDR	12/12 (100.0%)	5/5 (100.0%)

CEPH-R=cephalosporin-resistant; ESBL=extended-spectrum β-lactamases; MDR=multidrug resistance;
N=Number of subjects in the micro-ITT Population; N1=Number of subjects with a specific pathogen; n=Number of subjects with a clinical cure at the TOC visit

(1) Ditch et al, 2018 ASM Microbe Annual Meeting
(2) Comparators included ertapenem and meropenem for IGNITE1 and IGNITE4, respectively
(3) Data on file from IGNITE1 and IGNITE4 micro-ITT population

The most common adverse reactions that were reported in XERAVA-treated patients in IGNITE1 and IGNITE4 were infusion site reactions.

Selected Adverse Reactions Reported in ≥1% of Patients Receiving XERAVA[1]

	XERAVA (N=520)	Comparators[2] (N=517)
Infusion site reactions[3]	40 (7.7%)	10 (1.9%)
Nausea	34 (6.5%)	3 (0.6%)
Vomiting	19 (3.7%)	13 (2.5%)
Diarrhea	12 (2.3%)	8 (1.5%)
Hypotension	7 (1.3%)	2 (0.4%)
Wound dehiscence	7 (1.3%)	1 (0.2%)

(1) XERAVA FDA prescribing information
(2) Comparators included ertapenem and meropenem for IGNITE1 and IGNITE4, respectively
(3) Infusion site reactions include: catheter/vessel puncture site pain, infusion site extravasation, infusion site hypoaesthesia, infusion/injection site phlebitis, infusion site thrombosis, injection site/vessel puncture site erythema, phlebitis, phlebitis superficial, thrombophlebitis, and vessel puncture site swelling

Sales and Marketing Organization

We employ an experienced sales and marketing team dedicated to the commercialization of GIAPREZA and XERAVA. As of December 31, 2022, this team consisted of 35 professionals, including 27 critical care specialists.

Customers

During the year ended December 31, 2022, 503 hospitals in the U.S. purchased GIAPREZA, and 874 hospitals and other healthcare organizations in the U.S. purchased XERAVA. Hospitals and other healthcare organizations generally purchase our products through a network of specialty and wholesale distributors. These specialty and wholesale distributors are considered our

customers for accounting purposes. We do not believe that the loss of one of these distributors would significantly impact the ability to distribute our products, as we expect that sales volume would be absorbed by the remaining distributors. Due to the relatively short lead-time required to fill orders for GIAPREZA and XERAVA, backlog is not material to our business.

Competition

Catecholamines (primarily norepinephrine), which are available as generics and inexpensive, are typically used first line to treat distributive shock, while vasopressin, including Vasostrict® (Endo International plc) and vasopressin generic drugs, is typically used second line. In the randomized, Phase 3 study ATHOS-3, GIAPREZA demonstrated clinical benefit in patients who were not adequately responding to available vasopressors, including catecholamines and vasopressin. GIAPREZA's principal competition as a treatment in patients not adequately responding to available vasopressors is the use of these same vasopressors at increased doses. If we are unable to successfully change treatment practices, the commercial prospects for GIAPREZA will be limited, and our business may suffer.

XERAVA competes with a number of antibiotics that are currently marketed for the treatment of cIAI and other multidrug resistant infections, including: AVYCAZ (ceftazidime and avibactam, marketed by AbbVie Inc.); MERREM IV® (meropenem, marketed by AstraZeneca PLC); PRIMAXIN® (imipenem and cilastatin, marketed by Merck & Co., Inc.); RECARBRIO™ (imipenem, cilastatin, and relebactam, marketed by Merck & Co., Inc.); TYGACIL® (tigecycline, marketed by Pfizer Inc.); VABOMERE™ (meropenem and vaborbactam, marketed by Melinta Therapeutics, Inc.); ZERBAXA® (ceftolozane and tazobactam, marketed by Merck & Co., Inc.); ZOSYN® (piperacillin and tazobactam, marketed by Pfizer Inc.); and current and future generic versions of marketed antibiotics. If we are unable to successfully change treatment practices, the commercial prospects for XERAVA will be limited, and our business may suffer.

Regulatory Exclusivity

GIAPREZA and XERAVA are New Chemical Entities ("NCEs") approved by the U.S. FDA. In the U.S., NCEs approved by the FDA are eligible for market exclusivity under the U.S. Federal Food, Drug, and Cosmetic Act ("FDCA"), which can prevent the approval of generic versions of the NCE for 5 to 7.5 years from the date of the initial approval of the NCE. Specifically, the FDCA provides a 5-year period of marketing exclusivity within the U.S. to the applicant that gains approval of an NDA for an NCE. A drug is an NCE if the FDA has not previously approved any other new drug containing the same active moiety, which is the molecule or ion responsible for the action of the drug substance. During the exclusivity period, the FDA may not accept for review an Abbreviated New Drug Application ("ANDA") or a 505(b)(2) NDA submitted by another company for another version of such drug where the applicant does not own or have a legal right of reference to all of the data required for approval. However, an application may be submitted 4 years after the NDA approval of the NCE if it contains a certification of patent invalidity or non-infringement. Should the NDA holder commence litigation against the ANDA filer within 45 days of receipt of the certification notice, an automatic stay of the approval of any generic competition goes into effect until the earlier of: (i) 30 months from the receipt of the certification; or (ii) a court ruling of patent invalidity or non-infringement for the relevant patents. In the absence of a court ruling, the 30-month stay will be extended by such amount of time (if any) that is required for 7.5 years to have elapsed from the date of NDA approval of the NCE.

On February 15, 2022, La Jolla received a paragraph IV notice of certification (the "Notice Letter") from Gland Pharma Limited ("Gland") advising that Gland had submitted an Abbreviated New Drug Application ("ANDA") to the FDA seeking approval to manufacture, use or sell a generic version of GIAPREZA in the U.S. prior to the expiration of U.S. Patent Nos.: 9,220,745; 9,572,856; 9,867,863; 10,028,995; 10,335,451; 10,493,124; 10,500,247; 10,548,943; 11,096,983; and 11,219,662 (the "GIAPREZA Patents"), which are listed in the FDA's Approved Drug Products with Therapeutic Equivalence Evaluations (the "Orange Book"). The Notice Letter alleges that the GIAPREZA Patents are invalid, unenforceable and/or will not be infringed by the commercial manufacture, use or sale of the generic product described in Gland's ANDA.

On March 29, 2022, La Jolla filed a complaint for patent infringement of the GIAPREZA Patents against Gland and certain related entities in the United States District Court for the District of New Jersey in response to Gland's ANDA filing. In accordance with the Hatch-Waxman Act, because GIAPREZA is a new chemical entity and La Jolla filed a complaint for patent infringement within 45 days of receipt of the Notice Letter, the FDA cannot approve Gland's ANDA any earlier than 7.5 years from the approval of the GIAPREZA NDA unless the District Court finds that all of the asserted claims of the patents-in-suit are invalid, unenforceable and/or not infringed. We intend to vigorously enforce our intellectual property rights relating to GIAPREZA.

Under the Generating Antibiotic Incentives Now ("GAIN") provisions of the FDA Safety and Innovation Act ("FDASIA"), the FDA may designate a product as a qualified infectious disease product ("QIDP"). In order to receive this designation, a drug must qualify as an antibacterial or antifungal drug for human use intended to treat serious or life-threatening infections. We obtained a QIDP designation for the IV formulation of XERAVA for cIAI in July 2013. Upon approving an application for a QIDP, the FDA will extend by an additional 5 years any non-patent marketing exclusivity period awarded, such as a 5-year exclusivity period awarded for

an NCE. This extension is in addition to any pediatric exclusivity extension awarded. XERAVA has been awarded this 5-year exclusivity under FDASIA.

Our Product Candidates

The following table summarizes the status of our primary product candidates:

Product Candidate/ Indication	Preclinical	Ph 1	Ph 2	Ph 3	NDA	Program Status	Commercial Rights	Partnerships/ Grant Funding
Sulbactam-durlobactam (IV) Carbapenem-resistant *Acinetobacter* infections						U.S. NDA submitted Sep 2022, accepted for priority review Nov 2022	Worldwide excluding Asia-Pacific[1]	zai Lab
Zoliflodacin (Oral) Uncomplicated gonorrhea						Phase 3 trial ongoing – estimated enrollment completion in 2023	All developed countries[2]	NIH GARDP

(1) Zai Lab (Shanghai) Co., Ltd. ("Zai Lab") has licensed exclusive rights to SUL-DUR in the Asia-Pacific region.

(2) Global Antibiotic Research and Development Partnership ("GARDP") will fully fund the Phase 3 clinical trial and pharmaceutical development activities and has commercial rights in WHO defined low-income and specified middle-income countries. We have retained commercial rights in all major markets in North America, Europe and Asia-Pacific

SUL-DUR

Overview

Our lead product candidate, SUL-DUR, is a novel IV antibiotic. The product is a combination of sulbactam, a β-lactam antibiotic, and durlobactam, our novel β-lactamase inhibitor ("BLI") with broad spectrum β-lactamase coverage including Classes A, C and D, that we are developing for the treatment of a variety of serious infections caused by carbapenem-resistant *Acinetobacter*. We have completed three separate Phase 1 clinical trials, including one evaluating the penetration of SUL-DUR into the lung and one in renally impaired patients. Subsequently, we completed a Phase 2 clinical trial in patients with cUTIs. We initiated ATTACK, our single Phase 3 registration trial in 2019, that evaluated SUL-DUR in patients with confirmed carbapenem-resistant *Acinetobacter* pneumonia and/or bloodstream infections. We believe SUL-DUR has the ability to improve outcomes of patients with multidrug-resistant *Acinetobacter* infections, reducing their overall mortality. We announced positive top-line Phase 3 data in October 2021 and based on our positive top-line Phase 3 data and the totality of our preclinical and clinical data, we filed a new drug application ("NDA") with the FDA in September 2022. The NDA was accepted for filing by the U.S. FDA. We believe SUL-DUR has the ability to improve outcomes of patients with multidrug-resistant *Acinetobacter* infections, reducing their overall mortality.

Acinetobacter

Acinetobacter is a Gram-negative, opportunistic human pathogen that predominantly infects critically ill patients often resulting in severe pneumonia and bloodstream infections but can also infect other body sites as well. Once thought to be mostly benign, *Acinetobacter* is now considered a global threat in the healthcare setting due in part to its ability to acquire multidrug resistance at rates not previously seen in other bacteria. In addition, *Acinetobacter* has the ability to remain viable for up to 100 days in dry conditions and easily spreads via air or water droplets, which explains why the pathogen can often be found in many locations in the intensive care unit, or ICU, including bedrails, bedside tables, monitors of mechanical ventilators, intravenous pumps, door handles, stethoscopes and many other locations. Of significant concern, one study reported greater than 98% of *Acinetobacter* isolates in an ICU from non-clinical sources such as bedrails and door handles, were determined to be multidrug resistant.

Pneumonia and bloodstream infections caused by drug-resistant *Acinetobacter* can have mortality rates approaching 50%. Antibiotic-resistance rates of Acinetobacter to current standard-of-care treatments are some of the highest reported, between 30% and 50% in the United States and greater than 90% in parts of Europe and Asia. Acinetobacter resistance to β-lactams is primarily driven by the expression of Class D β-lactamases, often in combination with Class A and/or Class C β-lactamases. There are currently no effective antibiotics indicated for the treatment of multidrug-resistant *Acinetobacter* infections. Durlobactam is the first clinical-stage BLI with sufficient broad-spectrum activity against class A, C, and D β-lactamases to potentially restore the efficacy of β-lactam antibiotics against multidrug-resistant *Acinetobacter*.

Sulbactam, the β-lactam antibiotic used in SUL-DUR has superior microbiological potency against *Acinetobacter* compared to other β-lactam antibiotics based on *in vitro* and *in vivo* analyses. Historically, physicians used sulbactam to successfully treat *Acinetobacter* infections before development of broad β-lactamase mediated resistance rendered sulbactam on its own largely

ineffective. We believe our data demonstrates that combining durlobactam with sulbactam can effectively restore the activity of sulbactam against multidrug-resistant strains of *Acinetobacter*.

Market Opportunity

We estimate that there are up to 200,000 hospital-treated *Acinetobacter* infections annually in the United States and Europe, of which up to 100,000 are carbapenem-resistant *Acinetobacter* infections, which we regard as our initial target markets for SUL-DUR. We also believe there could be a significant market opportunity in Asia-Pacific, Central and South America, Russia and the Middle East given resistance rates exceeding 80% in some countries. If approved, we believe SUL-DUR has the potential to address the issues of resistance facing existing regimens, which is currently limiting the utility of the carbapenems, and tolerability, which is a concern with regimens containing colistin. There are currently no antibiotics indicated for the treatment of carbapenem-resistant *Acinetobacter* infections.

Clinical Development Plan

Completed Clinical Trials

Phase 3 registration trial: We completed ATTACK, a Phase 3 registration trial of SUL-DUR for the treatment of patients with carbapenem-resistant *Acinetobacter* infections, with positive top-line data announced in October 2021. ATTACK enrolled 207 patients at 95 clinical sites in 16 countries. This was a two-part trial with Part A being the randomized, comparative portion (SUL-DUR vs colistin) in patients with documented *Acinetobacter* hospital-acquired bacterial pneumonia (HABP), ventilator-associated bacterial pneumonia (VAPB), ventilated pneumonia (VP), or bacteremia, and Part B being an open-labeled portion including *Acinetobacter* infections resistant to, or having previously failed colistin or polymyxin B treatment. Baseline *Acinetobacter* isolates tested were greater than 95% carbapenem resistant.

SUL-DUR met the primary efficacy endpoint of 28-day all-cause mortality compared to colistin in the CRABC m-MITT population of Part A. SUL-DUR mortality was 19.0% (12/63) compared to 32.3% (20/62) in the colistin arm (treatment difference of -13.2%; 95% CI: -30.0, 3.5). Similar trends were demonstrated in 28-day and 14-day all-cause mortality favoring SUL-DUR across all study populations evaluated to date. A statistically significant difference in clinical cure at Test of Cure (TOC) was observed with 61.9% in SUL-DUR arm compared to 40.3% in the colistin arm (95% CI 2.9-40.3). In Part B, the 28-day all-cause mortality was 17.9% (5/28) and consistent with that observed in Part A.

Safety analyses from a total of 177 patients treated with SUL-DUR suggested that SUL-DUR was generally well-tolerated with a favorable safety profile compared to colistin. SUL-DUR met the primary safety objective with a statistically significant lower incidence of nephrotoxicity as measured by the RIFLE classification for acute kidney injury. SUL-DUR nephrotoxicity was 13.2% (12/91) versus 37.6% (32/85) in the colistin arm (p = 0. 0002). Overall adverse events (AEs) in the safety population were comparable between treatment groups with 87.9% (80/91) in the SUL-DUR arm vs. 94.2% (81/86) in the colistin arm in Part A, 89.3% (25/28) in Part B. Drug related AEs were 12.1% (10.7% in Part B) with SUL-DUR compared to 30.2% with colistin. The most common non-infectious AEs (≥10%) in the SUL-DUR arm were diarrhea (16.5%), allergic and hypersensitivity reactions (16.5%), anemia (13.2%) and hypokalemia (12.1%) in Part A. These AEs were also >10% in the colistin arm as was acute kidney injury.

On November 30, 2022, we announced that the U.S. FDA accepted for Priority Review the new drug application (NDA) for SUL-DUR. The FDA is currently planning to hold an advisory committee meeting to discuss this application. The target PDUFA date (or action date) is May 29, 2023.

Phase 2 clinical trial in cUTI patients: We completed a Phase 2 clinical trial in cUTI patients to provide additional safety and pharmacokinetic, or PK, data as well as efficacy data against carbapenem-resistant pathogens. Eighty patients were randomized to receive either a dose of SUL-DUR or placebo every six hours for seven days. Patients in both arms also received background therapy, which is current standard-of-care, with 500 mg of imipenem, or IMI, administered through IV every six hours. There were no serious adverse events reported and the adverse event profile of SUL-DUR plus IMI was similar to that of the IMI comparator arm. PK data observed in the Phase 2 trial was consistent with the PK data observed in the Phase 1 clinical trial in healthy volunteers.

We have completed three Phase 1 clinical trials, highlighted below, in addition to a Phase 2 clinical trial in patients with cUTIs. In all of these clinical trials, SUL-DUR was observed to be generally well tolerated.

Four-part Phase 1 first-in-human trial: Our four-part Phase 1 first-in-human clinical trial was conducted in Australia in 124 healthy volunteers. SUL-DUR was generally well tolerated, with no dose-related systemic adverse events or drug-related serious adverse events reported. SUL-DUR also exhibited linear dose-dependent increases in exposure and PK parameters across the dose range studied.

Phase 1 lung trial: Our Phase 1 lung trial assessed the concentration of SUL-DUR in lung fluid, an important metric to understand, because ATTACK includes patients with pneumonia and lack of appropriate lung tissue penetration has been found to contribute to reduced efficacy. We believe that the levels of SUL-DUR in the lung fluid achieved in this trial support its continued development as a potential treatment for pneumonia caused by *Acinetobacter*.

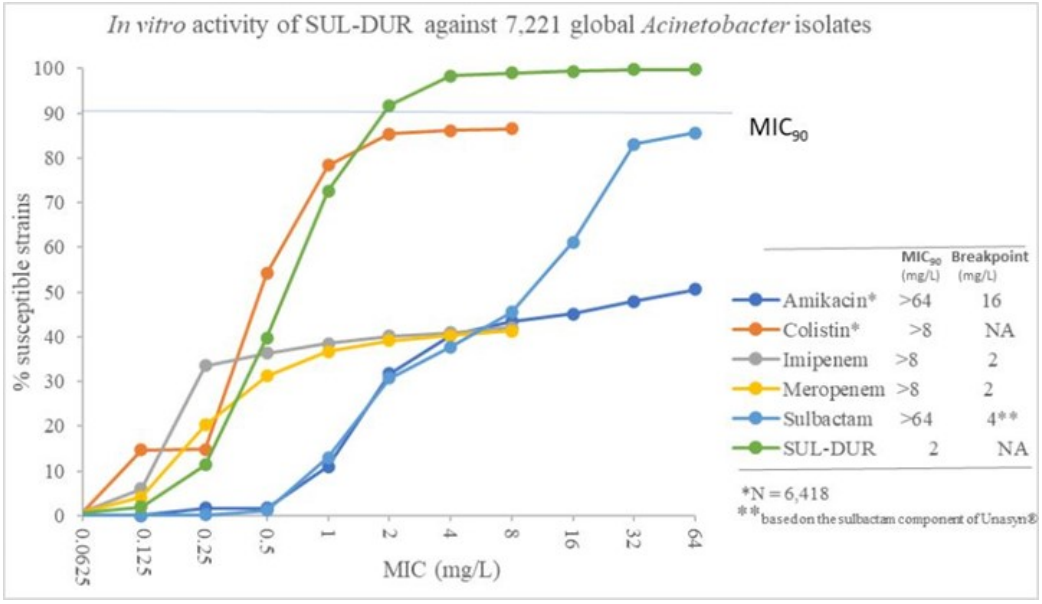
Phase 1 renal trial: Our Phase 1 renal trial analyzed serum levels in renally impaired patients and provided data to enable the development of a dose adjustment protocol for the type of patient targeted in our ongoing Phase 3 registration trial.

We submitted an IND for SUL-DUR to the U.S. FDA in June 2017, and the FDA notified us in July 2017 that we could proceed with this program. The FDA granted Fast Track and QIDP designation for SUL-DUR in September 2017 for the treatment of hospital-acquired and ventilator-acquired bacterial pneumonia and bloodstream infections due to *Acinetobacter*.

Global Acinetobacter Surveillance Data

Durlobactam has broad activity against a wide range of β-lactamases, including Classes A, C and D, unlike currently marketed BLIs that primarily cover only Class A and Class C β-lactamases. Durlobactam is the first BLI in clinical development with such a broad spectrum of *in vitro* activity.

SUL-DUR has also exhibited potent microbiological activity against *Acinetobacter* strains *in vitro.* Over a series of studies summarized in the figure below, we have compared the effectiveness of SUL-DUR, sulbactam alone and comparators in inhibiting 7,221 strains of *Acinetobacter* that were collected from patients around the world between 2011 and 2020. Amikacin and colistin were tested against 6,418 of the 7,221 strains. The plot in the figure below presents the cumulative percentage of these strains inhibited by increasing concentrations of each of the tested compounds. Sulbactam alone, as well as most of the other marketed antibiotics, had a very high MIC90 value of 64 mg/L, meaning that concentrations of 64 mg/L or greater were required to inhibit growth of 90% of the strains. The corresponding breakpoints, which are established by the Clinical & Lab Standards Institute, or CLSI, as the specified concentrations for each antibiotic that define whether a strain is considered resistant, are significantly lower than their MIC90 values. If the MIC90 of a drug is lower than its CLSI breakpoint, then that drug would be expected to be effective against more than 90% of the strains. If a drug's MIC90 is higher than its breakpoint, the drug would not be expected to have broad efficacy against those strains. This cumulative analysis suggests that recent global strains of *Acinetobacter* are resistant to all the comparator antibiotics other than colistin, consistent with their significantly diminished clinical utility against *Acinetobacter* infections. In contrast, SUL-DUR had very potent activity, with a much lower MIC90 of 2 mg/L. This is lower than the CLSI breakpoint for sulbactam, which is 4 mg/L (in Unasyn®, a combination of sulbactam and ampicillin), suggesting that our chosen target exposure levels of SUL-DUR may be effective against more than 90% of global, multidrug resistant *Acinetobacter* strains. A subset of 926 isolates out of the 7,221 strains tested were from Chinese hospitals collected in 2016-2018. 831 of the 926 (84.6%) Chinese isolates were carbapenem-resistant. In contrast, SUL-DUR showed potent activity against this subset, with an MIC90 of 2 mg/L and 97.9% of isolates susceptible to ≤ 4 mg/L of SUL-DUR.



Competition

We are initially developing SUL-DUR for the treatment of multidrug-resistant *Acinetobacter* infections. Due to rising resistance rates, standard-of-care treatment for multidrug-resistant *Acinetobacter* infections often includes a combination of several last-line treatment options, including carbapenems, tetracyclines, polymyxins, and other generically available agents. Despite using best available therapy, mortality rates of patients with multidrug-resistant *Acinetobacter* infections are reported as high as 50%. As of the date of this report, we are not aware of any marketed antibiotic that is indicated for the treatment of multidrug-resistant *Acinetobacter* infections; however, we are aware of other potentially competitive products that have shown *in vitro* activity against some strains of *Acinetobacter.* Melinta Therapeutics Inc. currently markets minocycline. Although recently approved for treating cUTIs, Fetroja®, from Shionogi & Co., Ltd., includes in its label a specific warning of an observed increase in all-cause mortality in patients with carbapenem-resistant Gram-negative bacterial infections that were treated with the drug. BioVersys AG reported in May 2022 that their lead program BV100, being developed specifically for multidrug-resistant *Acinetobacter* infections, completed three Phase 1 clinical trials.

Commercial Approach

In the United States, our commercial strategy is driven by our understanding of where *Acinetobacter* infections are known to exist. Given that *Acinetobacter* infections more commonly occur in immunocompromised patients, treatment settings for these patients are frequently large intensive care units (ICUs), specialized centers like transplant, cancer, and burn, outpatient long-term acute centers (LTACs) and home infusion.

SUL-DUR has been developed specifically for multi-drug resistant *Acinetobacter* infections and we believe the unmet need and value proposition of SUL-DUR will support its use for treating infections caused by this serious Gram-negative pathogen. This value proposition includes:

1. *Acinetobacter* infections currently cost lives. There is an urgent, global unmet medical need due to the limitations of currently available treatment options. Published mortality rates of *Acinetobacter* infections treated with best available therapy are reported to exceed 50%.
2. *Acinetobacter* infections currently cost time. These serious infections directly lead to time in a hospital where hospital length of stay is often measured in months or weeks instead of days.
3. *Acinetobacter* infections currently cost money. Given the limitations described above, carbapenem-resistant *Acinetobacter* infections are reported to be one of the costliest to treat, exceeding $75,000 per case based upon published literature.
4. We believe the data from ATTACK, combined with our overall preclinical and clinical data package, clearly demonstrate an efficacy and safety benefit of SUL-DUR over colistin in treating carbapenem resistant *Acinetobacter* infections.

Current *Acinetobacter* treatment protocols allow for clear positioning of SUL-DUR. Patients with suspected *Acinetobacter* infections are frequently treated with a broad-spectrum antibiotic, commonly a carbapenem, as first-line therapy. If susceptibility testing identifies that the causative bacterial pathogen is carbapenem-resistant *Acinetobacter*, the patient is then frequently switched to a colistin-based antibiotic regimen in an attempt to successfully treat the infection. Published literature, however, reports greater than 50% mortality rates using colistin-based regimens.

We believe that the data from the ATTACK Phase 3 registration trial demonstrate improved efficacy and safety profiles, that could result in SUL-DUR, if approved, being preferred to a colistin-based regimen for the treatment of multidrug-resistant, including carbapenem-resistant, *Acinetobacter* infections.

Multidrug-resistant *Acinetobacter* infections also present a significant unmet medical need in China and across the broader Asia/Pacific territory. Our collaboration and license agreement with Zai Lab, which included their participation in the ATTACK Phase 3 registration clinical trial, provides a potentially accelerated path for regulatory approval and commercialization in China and Asia-Pacific territories. Zai Lab supported the enrollment of approximately 25% of the evaluable patients in ATTACK from China, which we believe will support a regulatory submission in China. Under our agreement with Zai Lab, we receive upfront, milestone and royalty payments in addition to payment of certain Phase 3 registration clinical trial costs. We maintain 100% of the rights and associated economics in North America and Europe. Outside of the United States, we intend to work with multi-national pharmaceutical companies to leverage their commercialization capabilities in territories not covered by our agreement with Zai Lab. In January 2023, Zai Lab announced that the Center for Drug Evaluation of China's National Medical Products Administration has granted priority review status to the NDA for SUL-DUR for the treatment of infections caused by Acinetobacter baumannii, including multidrug-resistant and carbapenem-resistant (CRAB) strains.

Zoliflodacin

Overview

Our second late-stage product candidate is zoliflodacin, a potential single oral dose cure for the treatment of uncomplicated gonorrhea caused by the bacterial pathogen *N. gonorrhoeae*. Gonorrhea is an area of significant medical need and zoliflodacin is the only novel single dose treatment in development that provides a potential monotherapy oral alternative to intramuscular injections of ceftriaxone for the treatment of gonorrhea, including infections caused by drug-resistant strains. Zoliflodacin targets the validated mechanism of action of the fluoroquinolone class of antibiotics but does so in a novel manner to avoid existing fluoroquinolone resistance. We have completed several Phase 1 clinical trials and a Phase 2 clinical trial of zoliflodacin in patients with uncomplicated gonorrhea. In collaboration with GARDP, in 2019 we initiated a single Phase 3 registration trial of zoliflodacin in patients with uncomplicated gonorrhea. GARDP will fund all the Phase 3 clinical trial and pharmaceutical development costs and in return will receive commercial rights for zoliflodacin in WHO-defined low-income and select middle-income countries. We have retained commercial rights in all other countries, including the major markets in North America, Europe and Asia-Pacific.

Gonorrhea

Uncomplicated gonorrhea is an *N. gonorrhoeae* infection of the urethra, cervix, pharynx or rectum, and is more common than complicated gonorrhea, which includes spread of the infection to other tissues and potentially the bloodstream. Gonorrhea can be associated with serious complications, including pelvic inflammatory disease, ectopic pregnancy and infertility, as well as an increased risk of human immunodeficiency virus, or HIV. Despite the continued use of effective antibiotics, it remains one of the most common sexually transmitted bacterial infections in the world with an estimated 82.4 million people worldwide infected each year. The occasional absence of symptoms, more frequent in women, is thought to be one reason for sustained levels of infection. Antibiotics remain the mainstay for treating uncomplicated gonorrhea caused by *N. gonorrhoeae.*

N. gonorrhoeae is the bacterial pathogen responsible for gonorrhea and has a strong propensity for uptake of chromosomal DNA from other genera of *Neisseria* which allows the bacteria to accumulate many mutations in chromosomal genes leading to frequent resistance of antibiotics. For example, penicillin was introduced for *N. gonorrhoeae* infections in 1943, and initial resistance was reported in 1945. Fluoroquinolone antibiotics were first used to treat gonorrhea in 1949 and have been one of the most successful classes of antibiotics against *N. gonorrhoeae*, but even so resistance was identified in 1969. One member of this class, ciprofloxacin, was introduced in 1980 and resistance was identified in 1990. More recently cephalosporin antibiotics, notably cefixime, had been widely used for the treatment of gonorrhea due to their oral administration along with a favorable efficacy and safety profile, although resistance by *N. gonorrhoeae* has been reported since 2007. As widespread use of these antibiotics drove the emergence of drug-resistant *N. gonorrhoeae* strains, treatment guidelines have subsequently been amended. Ceftriaxone is currently the only CDC-recommended option for the treatment of gonorrhea and, until recently, was administered with azithromycin, a broad-spectrum antibiotic, to provide coverage against other sexually transmitted diseases that tend to occur concurrently with gonorrhea. However, rising resistance of *N. gonorrhoeae* to azithromycin recently prompted the CDC to now recommend 500mg ceftriaxone monotherapy. Ceftriaxone is administered by intramuscular injection, which can be painful and may require patient monitoring by a healthcare administrator. Although ceftriaxone remains effective in most of the U.S., in Hawaii and Massachusetts as well as in several countries, including China, Japan, Vietnam, South Korea, France and Spain, *N. gonorrhoeae* strains with resistance to azithromycin and ceftriaxone have been reported, prompting concerns that multidrug-resistant gonorrhea may become a major community health issue.

Market Opportunity

N. gonorrhoeae is an immediate global public health threat with 82.4 million cases worldwide in 2020 (WHO estimate). Cases of gonorrhea in the United States have reached an estimated 1.6 million per year. The WHO worldwide estimate of approximately 82.4 million new cases includes infected adolescents and adults aged 15–49 years. The CDC estimates that the cases of gonorrhea in the United States have been increasing at least 10% per year since 2009. In April 2021, the CDC announced that sexually transmitted diseases in the U.S. reached all-time high for 6th consecutive year, with approximately 2.6 million cases of chlamydia, gonorrhea & syphilis reported in 2019.

The results of a 2017-2018 survey of countries reporting decreased susceptibility, DS, or resistance, R, of *N. gonorrhoeae* to current antibiotics are reflected in the table below.

Antibiotic	Countries with DS or R
Oral ciprofloxicin	70/70 (100%)
Oral azithromycin	51/61 (84%)
Oral cefixime	24/51 (47%)
ceftriaxone	21/68 (31%)

Historically, to reduce the risk of spreading drug-resistant *N. gonorrhoeae*, the CDC has changed treatment guidelines when resistance rates to recommended first-line treatments reach 5%. Since 2015, there has only been one recommended treatment on CDC guidelines for gonorrhea: 250mg intramuscular injection of ceftriaxone plus 1g of oral azithromycin. In 2020 the CDC once again updated its treatment guideline, now recommending a 500mg intramuscular injection of ceftriaxone for treatment of uncomplicated gonorrhea. This follows a 2019 update in the United Kingdom where recommended empirical treatment of gonorrhea is now 1 g intramuscular ceftriaxone monotherapy.

Clinical Development Plan

Ongoing Registration Trial

Phase 3 registration trial: In 2019, we announced the initiation of a global, multi-center Phase 3 registration trial in collaboration with GARDP who is conducting and funding all Phase 3 clinical trial and pharmaceutical development costs. Up to 18 clinical trial sites are planned across the U.S., Thailand, South Africa, the Netherlands and Belgium. Our Phase 3 registration trial is a multi-center, open-label, noninferiority trial in approximately 1,000 enrolled patients with uncomplicated gonorrhea who will be randomized on a 2:1 basis to receive either a single 3.0g oral dose of zoliflodacin or a regimen of 500mg intramuscular ceftriaxone plus 1g oral azithromycin. The primary endpoint will be the proportion of patients with microbiological cure at urethral or cervical sites, approximately six days after treatment. The Data Safety Monitoring Board, or DSMB, in May 2021 recommended to continue the study without modification. Despite the ongoing challenges with the COVID-19 pandemic, we have observed an increase in the enrollment rate recently and based on current enrollment rates we anticipate completion of trial enrollment in 2023. Based on our discussions with the U.S. FDA, we believe that the efficacy data from this single Phase 3 registration trial, if positive, along with the data from our other clinical trials of zoliflodacin, will be sufficient to support the submission of an NDA to the U.S. FDA.

Completed Clinical Trials

Phase 2 clinical proof-of-concept trial: We have completed a multi-center, randomized, open-label Phase 2 clinical trial comparing a single oral dose of 2.0g or 3.0g of zoliflodacin to 500mg intramuscular ceftriaxone for the treatment of uncomplicated gonorrhea. In this trial, 179 randomized patients received treatment and zoliflodacin was generally well tolerated, with efficacy outcomes comparable to ceftriaxone. Microbiological eradication and clinical cure in urogenital infections with a single dose of zoliflodacin, the primary endpoint of the trial, was comparable to ceftriaxone, with 100% cure rate in both the 3.0g zoliflodacin and ceftriaxone groups in the per-protocol population. The results of this clinical trial were published in *The New England Journal of Medicine* in 2018.

Phase 1 clinical trial: We evaluated zoliflodacin in two Phase 1 clinical trials studying 72 healthy volunteers in total. In one trial, we evaluated PKs and tolerability in 48 subjects and food effects in 18 subjects, and in the second trial, we evaluated absorption, distribution, metabolism and excretion in six subjects. Zoliflodacin was generally well tolerated in these trials at doses we would expect to be clinically active for treating uncomplicated gonorrhea. Administration of a high-fat meal was associated with an increase in zoliflodacin plasma concentration, suggesting that zoliflodacin could be administered with or without food.

Preclinical Data

We have generated biochemical, microbiological and *in vivo* data on zoliflodacin. The data suggest that zoliflodacin retains potent activity against contemporary clinical isolates in the U.S., Europe, China, Thailand and South Africa that are resistant to other antibiotic classes including fluroquinolones, which was expected given its novel mechanism of action. In addition, the data show

significant resistance against two of the four standard antibiotics indicated for gonorrhea, ciprofloxacin, a fluoroquinolone, and azithromycin, a macrolide.

Competition

We are initially developing zoliflodacin as a single oral dose treatment for uncomplicated gonorrhea. Gonorrhea is commonly treated with 500mg intramuscular ceftriaxone, a generically available agent. Additional generic cephalosporins and fluoroquinolones are also prescribed, but not recommended as primary treatment options given current resistance rates. Gepotidacin, currently under development for a variety of infections by GlaxoSmithKline plc, is the only potentially competitive product candidate in late-stage clinical development that we are aware of that is being developed for the treatment of uncomplicated urogenital gonorrhea. A Phase 3 clinical trial (EAGLE-1) was initiated by GlaxoSmithKline in October 2019. A prior Phase 2 clinical trial revealed the emergence of resistance to gepotidacin in 2 urogenital microbiological failures following administration of a single oral dose. In an attempt to overcome this resistance, gepotidacin will be given in two oral doses in the EAGLE-1 clinical trial; a 4-tablet 3000 milligram (mg) oral dose at the study site followed by another 4-tablet 3000mg oral dose as an outpatient.

Commercial Approach

Antibiotics to treat uncomplicated gonorrhea will typically be available through primary care physicians, outpatient clinics and emergency rooms, and numerous community sites. In addition, placement on CDC guidelines has historically driven awareness and uptake in the U.S. We have partnered with GARDP who will lead the commercialization of zoliflodacin in certain WHO-defined low-income and specified middle-income countries.

Zoliflodacin is a potential single dose cure (sachet in water) that can facilitate “expedited partner therapy” at home, which may lower the chance for a repeat infection from a partner. Expedited partner therapy, or EPT, is the clinical practice of treating the sex partners of patients diagnosed with chlamydia or gonorrhea by providing prescriptions or medications to the patient to take to his/her partner without the health care provider first examining the partner. Within the United States, EPT is permissible in 45 states, potentially allowable in 4 states and is only prohibited in one state.

Manufacturing

Manufacturing of RELVAR®/BREO®ELLIPTA® (FF/VI) and ANORO® ELLIPTA® (UMEC/VI) is performed by GSK.

We rely on third-party manufacturers to produce GIAPREZA and XERAVA and expect to continue to do so in the foreseeable future to meet our development and commercial needs. In all of our manufacturing agreements, we require that contract manufacturers produce active pharmaceutical ingredients (“APIs”) and drug products in accordance with the FDA’s current Good Manufacturing Practices (“cGMPs”) and all other applicable laws and regulations. We maintain confidentiality agreements with potential and existing manufacturers in order to protect our proprietary rights related to GIAPREZA and XERAVA. The long-term commercial success of GIAPREZA and XERAVA will depend in part on the ability of our contract manufacturers to supply cGMP-compliant API and drug product without interruption.

With respect to our product candidates, we currently rely on third-party contract manufacturers for our required raw materials, drug substance, and finished drug product for our preclinical research and clinical trials. Although we have contracts with these third parties to meet our current clinical supply needs, we do not have any current contractual relationships with these third parties for the manufacture of commercial supply of our product candidates after they are approved. As our product candidates approach potential approval by any regulatory agency, we intend to enter into agreements with third-party contract manufacturers for the commercial production of those products. We currently employ internal resources to manage our manufacturing vendor relationships and processes.

Government Regulation

Government authorities in the United States, at the federal, state and local level, and in other countries extensively regulate, among other things, the research, development, testing, manufacture, packaging, storage, recordkeeping, labeling, advertising, promotion, distribution, marketing, post-approval monitoring and reporting, import and export of our products and reimbursement. The process of obtaining regulatory approvals and the subsequent compliance with applicable federal, state, local and foreign statutes and regulation require the expenditure of substantial time and financial resources.

U.S. Government Regulation

In the United States, the process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local statutes and regulations requires the expenditure of substantial time and financial resources. The failure to comply with the

applicable requirements at any time during the product development process, approval process or after approval may subject an applicant to a variety of administrative or judicial sanctions, such as the FDA's refusal to approve pending applications, withdrawal of an approval, imposition of a clinical hold, issuance of warning letters and untitled letters, product recalls, product seizures, total or partial suspension of production or distribution injunctions, fines, refusals of government contracts, restitution, disgorgement of profits or civil or criminal penalties.

Approval Processes

In the United States, the FDA regulates drugs under the Federal Food, Drug and Cosmetic Act, or the FDCA, the Public Health Service Act, or PHSA, and implementing regulations. The process of obtaining regulatory approvals and the subsequent compliance with applicable federal, state, local and foreign statutes and regulation require the expenditure of substantial time and financial resources. Failure to comply with the FDCA and other applicable U.S. requirements at any time during the product development process, approval process or after approval may subject us to a variety of administrative or judicial sanctions, any of which could have a material adverse effect on us. These sanctions could include:

- refusal to approve pending applications;
- withdrawal of an approval;
- imposition of a clinical hold;
- warning letters, untitled letters and similar communications;
- product seizures or recalls; or
- total or partial suspension of production or distribution, or injunctions, fines, restitution, disgorgement of profits or civil or criminal investigations and penalties brought by the FDA and the Department of Justice, or DOJ, or other

The process required by the FDA before a drug may be marketed in the United States generally involves the following:

- completion of preclinical laboratory tests, animal studies and formulation studies conducted according to Good Laboratory Practices or other applicable regulations;
- submission to the FDA of an IND application, which must become effective before human clinical trials may begin;
- approval by an independent institutional review board, or IRB, representing each clinical site before each clinical trial may be initiated;
- performance of adequate and well-controlled human clinical trials to establish the safety and efficacy of the proposed drug for its intended use, conducted in accordance with current good clinical practices, or cGCP, which are ethical and scientific quality standards and FDA requirements for conducting, recording and reporting clinical trials to assure that the rights, safety and well-being of trial participants are protected;
- preparation and submission to the FDA of an NDA;
- satisfactory completion of one or more FDA inspections of the manufacturing facility or facilities at which the product is produced to assess compliance with current good manufacturing practices, or cGMP, requirements to assure that the facilities, methods and controls are adequate to preserve the drug's safety, identity, strength, quality and purity; and
- FDA review and approval of the NDA.

Once a pharmaceutical candidate is identified for development, it enters the preclinical testing stage. Preclinical tests include laboratory evaluations of product chemistry, toxicity and formulation, as well as animal studies. An IND sponsor must submit the results of the preclinical tests, together with manufacturing information and analytical data, to the FDA as part of the IND. Some preclinical or nonclinical testing may continue even after the IND is submitted. In addition to including the results of the preclinical studies, the IND will also include one or more protocols detailing, among other things, the objectives of the clinical trial, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated if the first phase lends itself to an efficacy determination. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day time period, places the IND on clinical hold. In such a case, the IND sponsor and the FDA must resolve any outstanding concerns before clinical trials can begin. A clinical hold may occur at any time during the life of an IND and may affect one or more specific studies or all studies conducted u1nder the IND.

All clinical trials must be conducted under the supervision of one or more qualified investigators in accordance with cGCP. They must be conducted under protocols detailing, among other things, the objectives of the trial, dosing procedures, subject selection and

exclusion criteria and the safety and effectiveness criteria to be evaluated. Each protocol and any amendments must be submitted to the FDA as part of the IND, and progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA and more frequently in other situations, including the occurrence of serious adverse events. An IRB at each institution participating in the clinical trial must review and approve the protocol and any amendments before a clinical trial commences or continues at that institution, approve the information regarding the clinical trial and the informed consent form that must be provided to each trial subject or his or her legal representative, monitor the study until completed and otherwise comply with IRB regulations. Information about certain clinical trials must be submitted within specific timeframes to the National Institutes of Health for public dissemination on their ClinicalTrials.gov website.

Human clinical trials are typically conducted in three sequential phases that may overlap or be combined:

- Phase 1. The drug is initially introduced into healthy human subjects and tested for safety, dosage tolerance, absorption, distribution, metabolism and elimination. In the case of some products for severe or life-threatening diseases, such as multidrug-resistant infections, especially when the product may be inherently too toxic to ethically administer to healthy volunteers, the initial human testing is often conducted in patients with the target disease or condition.
- Phase 2. Clinical trials are initiated in a limited patient population intended to identify possible adverse effects and safety risks, to preliminarily evaluate the efficacy of the product for specific targeted diseases and to determine dosage tolerance and optimal dosage.
- Phase 3. Clinical trials are undertaken to further evaluate dosage, clinical efficacy and safety in an expanded patient population at geographically dispersed clinical study sites. These studies are intended to establish the overall risk-benefit ratio of the product and provide an adequate basis for regulatory approval and product labeling.

Phase 1, Phase 2 and Phase 3 testing may not be completed successfully within any specified period, if at all. The FDA or the sponsor may suspend or terminate a clinical trial at any time for a variety of reasons, including a finding that the research subjects or patients are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to patients.

During the development of a new drug, sponsors are given opportunities to meet with the FDA at certain points, including prior to submission of an IND, at the end of Phase 2 and before an NDA is submitted. Meetings at other times may also be requested. These meetings can provide an opportunity for the sponsor to share information about the data gathered to date, for the FDA to provide advice and for the sponsor and the FDA to reach agreement on the next phase of development. Sponsors typically use the end-of-Phase 2 meeting to discuss their Phase 2 clinical results and present their plans for the pivotal Phase 3 clinical trial or trials that they believe will support approval of the new drug.

The Pediatric Research Equity Act, or PREA, requires a sponsor to conduct pediatric studies for certain drugs and biologics. Specifically, PREA requires original NDAs, biologic license applications, or BLAs, and supplements thereto for a new active ingredient, new indication, new dosage form, new dosing regimen or new route of administration to contain a pediatric assessment unless the sponsor has received a deferral or waiver.

Concurrent with clinical trials, companies usually complete additional animal safety studies and must also develop additional information about the chemistry and physical characteristics of the drug and finalize a process for manufacturing the product in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the drug candidate and the manufacturer must develop methods for testing the quality, purity and potency of the final drugs. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the drug candidate does not undergo unacceptable deterioration over its shelf-life.

The results of product development, preclinical studies and clinical trials, along with descriptions of the manufacturing process, analytical tests conducted on the chemistry of the drug, proposed labeling and other relevant information are submitted to the FDA as part of an NDA requesting approval to market the product for one or more indications. The submission of an NDA is subject to the payment of user fees, but a waiver of such fees may be obtained under specified circumstances. The FDA reviews all NDAs submitted to ensure that they are sufficiently complete for substantive review before it accepts them for filing. It may request additional information rather than accept an NDA for filing. In this event, the NDA must be resubmitted with the additional information. The resubmitted application also is subject to completeness review before the FDA accepts it for filing.

Once the submission is accepted for filing, the FDA begins an in-depth review. NDAs receive either standard or priority review. A drug that, if approved, would represent a significant improvement in the safety or effectiveness of the treatment, prevention or diagnosis of a serious disease or condition may receive priority review. Requests for priority review generally must be submitted at the

time of NDA submission. The FDA has agreed to specified performance goals in the review process of NDAs. Under that agreement, 90% of applications seeking approval of new molecular entities, or NMEs, are meant to be reviewed within ten months from the date on which FDA accepts the NDA for filing, and 90% of applications for NMEs that have been designated for "priority review" are meant to be reviewed within six months of the filing date. For applications seeking approval of drugs that are not NMEs, the ten-month and six-month review periods run from the date that FDA receives the application. The review process may be extended by the FDA for three additional months to consider a major amendment to the application following the original submission.

The FDA reviews an NDA to determine, among other things, whether a product is safe and effective for its intended use and whether its manufacturing complies with cGMP requirements to assure and preserve the product's safety, identity, strength, quality and purity. The FDA may refer the NDA to an advisory committee for review and recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendation of an advisory committee, but it generally follows such recommendation.

Before approving an NDA, the FDA will typically inspect the facility or facilities where the product is manufactured and tested. These pre-approval inspections may cover all facilities associated with NDA submission, including drug component manufacturing (such as active pharmaceutical ingredients), finished drug product manufacturing, and control testing laboratories. Additionally, before approving an NDA, the FDA will typically inspect one or more clinical sites to assure compliance with cGCP. In addition, the FDA may require, as a condition of approval, risk evaluation and mitigation strategies, or REMS (which may include requirements for, restricted distribution and use), enhanced labeling, special packaging or labeling, expedited reporting of certain adverse events, pre-approval of promotional materials, restrictions on direct-to-consumer advertising or commitments to conduct additional research post-approval.

On the basis of the FDA's evaluation of the NDA and accompanying information, the FDA may issue an approval letter or a complete response letter. An approval letter authorizes commercial marketing of the product with specific prescribing information for specific indications. If the FDA ultimately decides that the NDA does not satisfy the criteria for approval, the FDA will issue a complete response letter to indicate that the agency will not approve the NDA in its present form. The complete response letter usually describes all of the specific deficiencies in the NDA identified by the FDA. If a complete response letter is issued, the applicant may either resubmit the NDA, addressing all of the deficiencies identified in the letter, or withdraw the application.

Expedited Review and Approval

The FDA has various programs, including Fast Track and priority review, which are intended to expedite or simplify the process for developing and/or reviewing drugs. Even if a drug qualifies for one or more of these programs, the FDA may later decide that the drug no longer meets the conditions for qualification or that the time period for FDA review or approval will not be shortened. Generally, drugs that may be eligible for these programs are those for serious or life-threatening conditions, those with the potential to address unmet medical needs and those that offer meaningful benefits over existing treatments. For example, Fast Track is a process designed to facilitate the clinical development and expedite the review of drugs to treat serious diseases with the potential, based on nonclinical or clinical data, to fill an unmet medical need. Priority review is designed to give drugs that offer a significant improvement in safety or effectiveness of treatment for a serious condition an expedited review within eight months from the completed submission (six months from filing) as compared to a standard review time of twelve months from the completed submission (10 months from filing) for a standard new molecular entity NDA. Although Fast Track and priority review do not affect the standards for approval, the FDA will attempt to facilitate early and frequent meetings with a sponsor of a Fast Track designated drug and expedite review of the application for a drug designated for priority review.

The Generating Antibiotic Incentives Now Act, or GAIN Act, is intended to provide incentives for the development of new QIDPs. A new drug that is designated as a QIDP after a request by the sponsor that is made before an NDA is submitted will be eligible, if approved, for an additional five years of exclusivity beyond any period of exclusivity to which it would have previously been eligible. In addition, a QIDP will receive priority review and qualify for a Fast Track designation. QIDPs are defined as antibacterial or antifungal drugs intended to treat serious or life-threatening infections, including those caused by an antibacterial or antifungal resistant pathogen or qualifying pathogens identified by the FDA. XERAVA and SUL-DUR have been designated by the FDA as a QIDP. Zoliflodacin has also been designated as a QIDP by the FDA for the treatment of uncomplicated gonorrhea.

Patent Term Restoration and Data Exclusivity

Depending upon the timing, duration and specifics of FDA approval of the use of our drugs, some of our U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, commonly referred to as the Hatch-Waxman Amendments. As noted above, the Hatch-Waxman Amendments permit a patent restoration term of up to five years for a single patent for an approved product as compensation for patent term lost during product development and the FDA regulatory review process. However, patent term restoration cannot extend the remaining term of a patent beyond a total of 14

years from the product's approval date and only those claims covering such approved drug product, a method for using it or a method for manufacturing it may be extended. Only one patent applicable to an approved drug is eligible for the extension and the application for the extension must be submitted prior to the expiration of the patent. The USPTO, in consultation with the FDA, reviews and approves the application for any patent term extension or restoration. We have applied for restoration of patent term for one U.S. Patent covering XERAVA and, in the future, we may apply for restoration of patent term for other currently owned or licensed patents to add patent life beyond its current expiration date, depending on the expected length of the clinical trials and other factors involved in the filing of the relevant NDA.

Data exclusivity provisions under the FDCA also can delay the submission or the approval of certain applications. The FDCA provides a five-year period of non-patent data exclusivity within the United States to the first applicant to gain approval of an NDA for a new chemical entity. A drug is a new chemical entity if the FDA has not previously approved any other new drug containing the same active moiety, which is the molecule or ion responsible for the action of the drug substance. During the exclusivity period, the FDA may not accept for review an abbreviated new drug application, or ANDA, or a 505(b)(2) NDA submitted by another company using the drug entitled to data exclusivity as the reference listed drug, or RLD. However, an application may be submitted after four years if it contains a certification of patent invalidity or non-infringement. The FDCA also provides three years of data exclusivity for an NDA, 505(b)(2) NDA or supplement to an existing NDA if new clinical investigations, other than bioavailability studies, that were conducted or sponsored by the applicant are deemed by the FDA to be essential to the approval of the application, for example, for new indications, dosages or strengths of an existing drug. This three-year exclusivity covers only the use or conditions of use associated with the new clinical investigations and does not prohibit the FDA from approving ANDAs for drugs containing the original active agent for other uses or conditions of use. Five-year and three-year exclusivity will not delay the submission or approval of a full NDA. However, an applicant submitting a full NDA would be required to conduct its own preclinical and clinical studies in support of its application or obtain a right of reference to all of the preclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness.

In addition, as described above, under the GAIN Act a new drug that is designated as a QIDP is eligible for an additional five years of exclusivity to be added to certain other exclusivity periods that the application may qualify for upon approval, specifically five-year exclusivity, three-year exclusivity, and orphan exclusivity.

Pediatric Exclusivity

The Best Pharmaceuticals for Children Act provides for an additional six months of exclusivity, which is added on to patent and exclusivity periods in effect at the time the pediatric exclusivity award is granted, if a sponsor conducts clinical trials in children in response to a written request from the FDA, or a Written Request. The FDA may request studies on approved indications in separate Written Requests. The issuance of a Written Request does not require the sponsor to undertake the described studies. To date, we have not received any Written Requests.

Post-approval Requirements

Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems, including safety issues, with a product may result in restrictions on the product or even complete withdrawal of the product from the market. After approval, some types of changes to the approved product, such as adding new indications, manufacturing changes and additional labeling claims, are subject to further FDA review and approval. In addition, the FDA may require testing and surveillance programs to monitor the effect of approved products that have been commercialized, and the FDA has the power to prevent or limit further marketing of a product based on the results of these post-marketing programs. The FDA and other authorities also strictly regulate the promotional claims that may be made about prescription products. Under the FDCA the sponsor of an approved drug in the United States may not promote that drug for unapproved, or off-label, uses, although a physician may prescribe a drug for an off-label use in accordance with the practice of medicine. If we are found to have promoted off-label uses, we may be subject to significant liability, including sanctions, civil and criminal fines and penalties, and injunctions prohibiting us from engaging in specified promotional conduct.

Moreover, any drug products manufactured or distributed pursuant to FDA approvals are subject to continuing regulation by the FDA, including, among other things:

- record-keeping requirements;
- reporting of adverse experiences with the drug;
- providing the FDA with updated safety and efficacy information;

- drug sampling and distribution requirements;
- notifying the FDA and gaining its approval of specified manufacturing or labeling changes;
- complying with certain electronic records and signature requirements; and
- complying with FDA promotion and advertising requirements.

Drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to register their establishments with the FDA and certain state agencies and are subject to periodic unannounced inspections by the FDA and some state agencies for compliance with cGMP requirements and other laws.

Failure to comply with the FDCA and other applicable U.S. requirements at any time during the product development process, approval process or after approval may subject us to a variety of administrative or judicial sanctions, any of which could have a material adverse effect on us. These sanctions could include:

- refusal to approve pending applications;
- withdrawal of an approval;
- imposition of a clinical hold;
- warning letters, untitled letters and similar communications;
- product seizures or recalls;
- total or partial suspension of production or distribution; or
- injunctions, fines, restitution, disgorgement of profits or civil or criminal investigations and penalties brought by the FDA and DOJ, or other governmental entities.

From time to time, legislation is drafted, introduced and passed in Congress that could significantly change the statutory provisions governing the approval, manufacturing and marketing of products regulated by the FDA. In addition, FDA regulations and guidance are often revised or reinterpreted by the agency in ways that may significantly affect our business and our products. It is impossible to predict whether legislative changes will be enacted, or FDA regulations, guidance or interpretations changed or what the impact of such changes, if any, may be.

Foreign Regulation

In addition to regulations in the United States, we will be subject to a variety of foreign regulations governing clinical trials and commercial sales and distribution of our products. Whether or not we obtain FDA approval for a product, we must obtain approval by the comparable regulatory authorities of foreign countries or economic areas, such as the EU, before we may commence clinical trials or market products in those countries or areas. The approval process and requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary greatly from place to place, and the time may be longer or shorter than that required for FDA approval.

Under EU regulatory systems, a company may submit marketing authorization applications under the centralized, decentralized or mutual recognition procedures, or under the purely national route of approval. The centralized procedure is compulsory for medicinal products produced by biotechnology or those medicinal products containing new active substances for specific indications such as the treatment of acquired immune deficiency syndrome, or AIDS, cancer, neurodegenerative disorders, diabetes, viral diseases, and designated orphan medicines, and is optional for other medicines that are highly innovative. Under the centralized procedure, a marketing application is submitted to the European Medicines Agency, or EMA, where it will be evaluated by the relevant scientific committee, in most cases the Committee for Medicinal Products for Human Use, and a favorable opinion typically results in the grant by the European Commission of a single marketing authorization that is valid for all EU member states and, by extension (after national implementing measures), in Norway, Iceland and Liechtenstein. In general, an initial marketing authorization is valid for five years, but once renewed is usually valid for an unlimited period. The decentralized procedure allows marketing authorization applications to be submitted simultaneously in two or more EU member states, whereas the mutual recognition procedure must be used if the product has already been authorized in at least one other EU member state. Both the decentralized and mutual recognition procedures provide for approval by one or more "concerned" member states based on an assessment of an application performed by one-member state, known as the "reference" member state.

Under the decentralized approval procedure, an applicant submits an application, or dossier, and related materials to the reference member state and concerned member states. The reference member state prepares a draft assessment and drafts of the related materials within 120 days after receipt of a valid application. Within 90 days of receiving the reference member state's assessment report, each

concerned member state must approve the assessment report and related materials, unless they identify a serious risk to public health. Under the mutual recognition procedure, the concerned member states have the same 90-day period to recognize the marketing authorization in the reference member state. In either case, concerns about serious risks to public health escalate through the relevant EMA scientific committees, and the disputed points may eventually result in a consensus opinion from the Committee for Medicinal Products for Human Use that is referred to the European Commission, whose decision is binding on all member states. The purely national procedure results in a marketing authorization in a single EU member state.

Following the result of a referendum in 2016, the United Kingdom left the EU on January 31, 2020, and as of January 1, 2021, the United Kingdom and EU operate separate regulatory regimes. The UK and EU announced on December 24, 2020, that they had agreed a Trade and Cooperation Agreement, or TCA, to govern their future relationship. The TCA remains provisional until formally ratified by the EU. The TCA sets out the new arrangements for trade of goods, including medicines and medical devices, which aims to ensure goods continue to flow between the EU and the UK and also has implications for product regulation and mutual recognition.

As a result of the United Kingdom's departure from the EU, if a company wishes to sell its products in the United Kingdom, it will need to seek and maintain appropriate national marketing authorizations. The TCA does not provide for wholesale mutual recognition of the regulatory regimes and so products exported from the UK to the EU must comply with the EU's regulatory requirements. In the pharmaceutical context, this has had a number of implications. From January 31, 2020, the UK no longer participated in EU institutions and their decision-making, including approval decisions under the centralized procedure. Moreover, the movement of finished pharmaceutical products into the EU from the UK is treated as an import from a third country. Since the TCA does not provide for mutual recognition of batch testing and release, products must be quality control tested and released in the EU. However, the UK will unilaterally waive batch testing requirements for UK imports from the EU for products placed on the market before January 2023. It remains to be seen how these developments will impact regulatory requirements for product candidates and products in the United Kingdom.

Reimbursement

Significant uncertainty exists as to the coverage and reimbursement status of products approved by the FDA and other government authorities. Sales of products will depend, in part, on the extent to which third-party payors, including government health programs in the United States such as Medicare and Medicaid, commercial health insurers and managed care organizations, provide coverage, and establish adequate reimbursement levels for, such products. The process for determining whether a payor will provide coverage for a product may be separate from the process for setting the price or reimbursement rate that the payor will pay for the product once coverage is approved. Third-party payors are increasingly challenging the prices charged, examining the medical necessity, and reviewing the cost-effectiveness of medical products and services and imposing controls to manage costs. Third-party payors may limit coverage to specific products on an approved list, or formulary, which might not include all the approved products for a particular indication. For example, in the U.S. and most major foreign markets, drugs like GIAPREZA and XERAVA that are administered in the hospital must be purchased by the hospital and generally are not reimbursed by third-party payors. Hospitals instead are reimbursed for patient cases based on patients' diagnosed conditions under the U.S. Medicare diagnosis-related group ("DRG") system or other like systems for non-Medicare patients in the U.S. and in most major foreign markets. Adoption of new drugs that are administered in the hospital generally occurs more slowly than adoption of new drugs that are taken on an outpatient basis, which generally are paid for by third-party payors.

To secure coverage and reimbursement for any product that might be approved for sale, a company may need to conduct expensive pharmacoeconomic studies to demonstrate the medical necessity and cost effectiveness of the product, in addition to the costs required to obtain FDA or other comparable regulatory approvals. Nonetheless, product candidates may not be considered medically necessary or cost effective. Additionally, a payor's decision to provide coverage for a drug product does not imply that an adequate reimbursement rate will be approved. Further, one payor's determination to provide coverage for a drug product does not ensure that other payors will also provide coverage for the drug product. Third-party reimbursement may not be sufficient to maintain price levels high enough to realize an appropriate return on investment in product development.

Health Care Laws Governing Interactions with Healthcare Providers

In addition to FDA restrictions on marketing of pharmaceutical products, several other types of state and federal laws restrict our business activities, including certain marketing practices. These laws include, without limitation, anti-kickback laws, false claims laws, data privacy and security laws, as well as transparency laws regarding payments or other items of value provided to healthcare providers.

The federal Anti-Kickback Statute prohibits, among other things, knowingly and willfully offering, paying, soliciting or receiving remuneration to induce or in return for purchasing, leasing, ordering or arranging for the purchase, lease or order of any healthcare item, good, facility or service reimbursable under Medicare, Medicaid or other federal healthcare programs. The term "remuneration"

has been broadly interpreted to include anything of value. This statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand and prescribers, purchasers and formulary managers, among others, on the other. Although there are several statutory exceptions and regulatory safe harbors protecting certain common activities from prosecution or other regulatory sanctions, the exceptions and safe harbors are drawn narrowly, and practices that involve remuneration that are alleged to be intended to induce prescriptions, purchases or recommendations may be subject to scrutiny if they do not qualify for an exception or safe harbor. Failure to meet all requirements of a particular applicable statutory exception or regulatory safe harbor does not make the conduct per se illegal under the federal Anti-Kickback Statute. Instead, the legality of the arrangement will be evaluated on a case-by-case basis based on a cumulative review of all its facts and circumstances. Several courts have interpreted the statute's intent requirement to mean that if any one purpose of an arrangement involving remuneration is to induce referrals of federal healthcare covered business, the federal Anti-Kickback Statute has been violated. Additionally, the intent standard under the federal Anti-Kickback Statute was amended by the Patient Protection and Affordable Care Act of 2010, as amended by the Health Care and Education Reconciliation Act of 2010, collectively the Affordable Care Act, or ACA, to a stricter standard such that a person or entity no longer needs to have actual knowledge of the statute or specific intent to violate it in order to have committed a violation. In addition, the ACA codified case law that a claim for payment for items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the federal civil False Claims Act.

Federal false claims laws, including the civil False Claims Act, and civil monetary penalties laws prohibit any person or entity from, among other things, knowingly presenting, or causing to be presented, a false claim for payment to the federal government, or knowingly making, or causing to be made, a false statement to have a claim paid. Pharmaceutical and other healthcare companies have been prosecuted under these laws for, among other things, allegedly inflating drug prices they report to pricing services, which in turn were used by the government to set Medicare and Medicaid reimbursement rates, and for allegedly providing free product to customers with the expectation that the customers would bill federal programs for the product. In addition, certain marketing practices, including off-label promotion, have also been alleged to violate false claims laws.

The federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, created additional federal criminal and civil statutes that prohibit among other actions, knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program, including private third-party payors, knowingly and willfully embezzling or stealing from a healthcare benefit program, willfully obstructing a criminal investigation of a healthcare offense, and knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services. As with the federal Anti-Kickback Statute, the ACA amended the intent standard for certain healthcare fraud under HIPAA such that a person or entity no longer needs to have actual knowledge of the statute or specific intent to violate it to have committed a violation.

In addition, we may be subject to data privacy and security regulations promulgated by both the federal government and the states in which we conduct our business. HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or HITECH, and its implementing regulations, impose certain requirements on covered entities (i.e., certain healthcare providers, health plans and healthcare clearinghouses) relating to the privacy, security and transmission of individually identifiable health information. Among other things, HITECH makes HIPAA's security standards directly applicable to business associates, independent contractors or agents of covered entities that receive or obtain protected health information in connection with providing a service on behalf of a covered entity. HITECH also created four new tiers of civil monetary penalties, amended HIPAA to make civil and criminal penalties directly applicable to business associates, and gave state attorneys general new authority to file civil actions for damages or injunctions in federal courts to enforce the federal HIPAA laws and seek attorneys' fees and costs associated with pursuing federal civil actions.

What is more, the federal Physician Payments Sunshine Act, created under the ACA, and its implementing regulations, require certain manufacturers of drugs, devices, biologicals and medical supplies for which payment is available under Medicare, Medicaid or the children's health insurance program (with certain exceptions) to annually report information related to certain payments or other transfers of value provided to covered recipients, including physicians, as defined by such law, and teaching hospitals, or to entities or individuals at the request of, or designated on behalf of, the physicians and teaching hospitals' covered recipients and information related to certain ownership and investment interests held by physicians and their immediate family members.

The majority of states also have statutes or regulations similar to the aforementioned federal laws, some of which are broader in scope and apply to items and services reimbursed under Medicaid and other state programs, or, in several states, apply regardless of the payor. Some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government. In addition, some state laws require drug manufacturers to report information related to payments to clinicians and other healthcare providers or marketing expenditures and drug pricing. Further, some state and local laws require the licensure of pharmaceutical sales representatives. State and foreign laws also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Finally, in Europe, the European Union General Data Protection Regulation (2016/679) ("GDPR") contains provisions specifically directed at the processing of health information. The GDPR provides for potentially significant sanctions and contains extraterritoriality measures intended to bring non-EU companies under the regulation. In addition to the GDPR, individual countries in Europe and elsewhere in the world have enacted similar data privacy legislation. This legislation imposes increased compliance obligations and regulatory risk, including the potential for significant fines for noncompliance.

Healthcare and Other Reform

In the United States, there have been and continue to be a number of significant legislative initiatives to contain healthcare costs. Federal and state governments continue to propose and pass legislation designed to reform delivery of, or payment for, healthcare, which include initiatives to reduce the cost of healthcare. For example, in March 2010, the United States Congress enacted the ACA, which expanded health care coverage through Medicaid expansion and the implementation of the individual mandate for health insurance coverage and which included changes to the coverage and reimbursement of drug products under government healthcare programs. Under the Trump administration, there were ongoing efforts to modify or repeal all or certain provisions of the ACA. For example, tax reform legislation was enacted at the end of 2017 that eliminated the tax penalty established under the ACA for individuals who do not maintain mandated health insurance coverage beginning in 2019. The ACA has also been subject to judicial challenge. In December 2018, a federal district court, in a challenge brought by a number of state attorneys general, found the ACA unconstitutional in its entirety because, once Congress repealed the individual mandate provision, there was no longer a basis to rely on Congressional taxing authority to support enactment of the law. In December 2019, the federal appellate court upheld the district court ruling that the individual mandate was unconstitutional and remanded the case back to the district court to determine whether the remaining provisions of the ACA are invalid as well. The case has been appealed to the U.S. Supreme Court where a ruling remains pending.

There were other reform initiatives under the former Trump Administration, including initiatives focused on drug pricing. For example, the Bipartisan Budget Act of 2018 contained various provisions that affect coverage and reimbursement of drugs, including an increase in the discount that manufacturers of Medicare Part D brand name drugs must provide to Medicare Part D beneficiaries during the coverage gap from 50% to 70% starting in 2019. As another example, in 2018, President Trump and the Secretary of the HHS, released a "blueprint" to lower prescription drug prices and out-of-pocket costs. Certain proposals in the blueprint, and related drug pricing measures proposed since the blueprint, could cause significant operational and reimbursement changes for the pharmaceutical industry. HHS has solicited feedback on some of these measures and, at the same, has implemented others under its existing authority. On November 20, 2020, CMS issued an interim final rule through the CMS Innovation Center whereby Medicare Part B reimbursement for "certain high-cost prescriptions drugs" would be no more than most-favored-nation price (i.e., the lowest price) after adjustments, for a pharmaceutical product that the drug manufacturer sells in a member country of the Organization for Economic Cooperation and Development that has a comparable per-capita gross domestic product. On December 28, 2020, the United States District Court in Northern California issued a nationwide preliminary injunction against implementation of the interim final rule. While some of these and other measures may require additional authorization to become effective, members of Congress and the new Biden administration have indicated that lowering prescription drug prices is a priority, but it is not yet clear what steps the Biden Administration will take or whether such steps will be successful.

There have also been recent state legislative efforts to address drug costs, which generally have focused on increasing transparency around drug costs or limiting drug prices and address price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing.

In 2019, the DISARM Act of 2019 was introduced in Congress as new legislation to provide financial incentives for pharmaceutical companies to develop new antibiotics. This new legislation was guided by input from the IDSA and will help to ensure that patients can access new antibiotics when they are clinically appropriate, require hospitals to establish antibiotic stewardship programs, and spur improved reporting of antibiotic use and resistance to more rapidly identify challenges and inform best practices. More recently, this legislation was reintroduced in the U.S. House of Representatives in June 2021 which aims to amend title XVIII of the Social Security Act to encourage the development and use of DISARM antimicrobial drugs, and for other purposes.

General legislative cost control measures may also affect reimbursement for our product candidates. The Budget Control Act, as amended, resulted in the imposition of 2% reductions in Medicare, but not Medicaid, payments to providers in 2013 and will remain in effect through 2029 unless additional Congressional action is taken. There was a temporary suspension of the 2% reduction during the pandemic; that temporary suspension is scheduled to expire on March 31, 2021. Any significant spending reductions affecting Medicare, Medicaid or other publicly funded or subsidized health programs that may be implemented and/or any significant taxes or fees that may be imposed on us could have an adverse impact on our results of operations.

Legislation was introduced to the U.S. Senate in September 2020 which aims to reinvigorate innovation for the development of new antibiotics through a subscription contract program managed by HHS. The PASTEUR Act was introduced to provide a mechanism for funding designated 'critical need antimicrobial' drugs post FDA approval. In return, patients covered by federal insurance programs will receive these drugs at no cost. These Contracts under the PASTEUR Act could range from $750 million to $3 billion in value. It is unclear when or if the PASTEUR Act or similar incentive programs will become law. In October 2021, the PACCARB authored a letter to the Honorable Xavier Becerra, Secretary, Department of Health and Human Services recommending the passage of both DISARM and PASTEUR and the antimicrobial stewardship provisions contained within each act.

Adoption of new legislation at the federal or state level could affect demand for, or pricing of, our current or future products if approved for sale. We cannot, however, predict the ultimate content, timing or effect of any changes to the ACA or other federal and state reform efforts. There is no assurance that federal or state health care reform will not adversely affect our future business and financial results.

Other Laws and Regulations

We are subject to a variety of financial disclosure and securities trading regulations as a public company in the U.S., including laws relating to the oversight activities of the U.S. Securities and Exchange Commission ("SEC") and the regulations of the Nasdaq Capital Market, on which our shares of common stock are traded. We are also subject to various laws and regulations relating to safe working conditions, laboratory practices and the experimental use of animals.

Intellectual Property

Our commercial success depends in part on our ability to obtain and maintain proprietary or intellectual property protection for our product candidates, our core technologies, and other know-how. To accomplish this we rely on the skills, knowledge and experience of our scientific and technical personnel, as well as that of our advisors, consultants and other contractors. To help protect our proprietary know-how that is not patentable, we rely on trade secret protection and confidentiality agreements to protect our interests. We require our employees, consultants and advisors to enter into confidentiality agreements prohibiting the disclosure of confidential information and requiring disclosure and assignment to us of the ideas, developments, discoveries and inventions important to our business. We file patent applications directed to our key product candidates to establish intellectual property positions. These patent applications are intended to protect new chemical entities relating to these product candidates as well as their manufacturing processes, intermediates and uses in the treatment of diseases.

The intellectual property portfolios for our commercial products, advanced product candidates, and various compounds are summarized below.

GIAPREZA

As of February 15, 2023 , the licensed intellectual property portfolio relating to GIAPREZA® included 12 issued U.S. patents, 2 pending U.S. patent applications, 8 issued foreign patents and 15 pending foreign patent applications. The issued U.S. patents, and patents that may issue from the pending U.S. patent applications, will expire between 2029 and 2034, absent any disclaimers, extensions, or adjustments of patent term. The foreign patents, and patents that may issue from the pending foreign patent applications, will expire in 2034, absent any disclaimers, extensions, or adjustments of patent term.

As of February 15, 2023, the intellectual property portfolio relating to GIAPREZA included 3 issued U.S. patents, 8 pending U.S. patent applications, 7 issued foreign patents and 10 pending foreign patent applications. The issued U.S. patents, and patents that may issue from the pending U.S. patent applications, will expire between 2034 and 2044, absent any disclaimers, extensions, or adjustments of patent term. The foreign patents, and patents that may issue from the pending foreign patent applications, will expire between 2034 and 2044, absent any disclaimers, extensions, or adjustments of patent term.

XERAVA

As of February 15, 2023, we owned 2 issued U.S. patents, 1 pending U.S. patent application, 17 issued foreign patents and 4 pending foreign patent applications relating to XERAVA. The issued U.S. patents, and the patent that may issue from the pending U.S. patent application, will have an expiration date of August 7, 2029, absent any disclaimers, extensions, or adjustments of patent term. The term of 1 of the U.S. patents has received 508 days of patent term adjustment. The foreign patents, and patents that may issue from the pending foreign applications, will likewise have an expiration date of August 7, 2029, absent any disclaimers, extensions, or adjustments of patent term.

As of February 15, 2023, we also filed applications for Supplementary Protection Certificates based on European Patent No. 2323972 covering the composition of matter and use of XERAVA. Some applications have been granted and others are pending.

In addition, as of February 15, 2023, we also owned 2 issued U.S. patent, 1 pending U.S. patent application and 11 pending foreign patent applications that relate to crystalline forms of eravacycline, any U.S. patent that may issue from the pending patent application will expire in 2037 absent any disclaimers, extensions, or adjustments of patent term. Likewise, any foreign patents that may issue from the pending foreign patent applications will expire in 2037. We also owned 5 issued U.S. patents, 1 pending U.S. patent application, 32 issued foreign patents and 17 pending foreign patent applications relating to other tetracycline-related intellectual property.

	United States			Foreign		
Description	Issued	Pending	Expiration	Issued	Pending	Expiration
GIAPREZA	15	10	2029 - 2044	15	25	2034 - 2044
XERAVA	4	2	2029 - 2037	17	15	2029 - 2037
Other	5	1	2030 - 2037	32	17	2033 - 2037

Durlobactam

Our intellectual property portfolio for our durlobactam program contains patent applications directed to compositions of matter for durlobactam and other chemical analogs, as well as methods of making, referred to as synthetic methods, and methods of use and modes of treatment using durlobactam in combination with one or more antibiotic compounds. As of February 15, 2023, we owned four issued U.S. patents, one pending provisional application, one pending PCT application, 107 issued foreign patents as well as six pending foreign patent applications, of which two are allowed. The issued foreign patents are in several jurisdictions including Australia, the European Union, Canada, China, Hong Kong, Israel, India, Japan, Macau, Mexico, New Zealand, the Philippines, the Russian Federation, Singapore, South Africa, South Korea, Taiwan and the United Kingdom. Issued U.S. and foreign patents and patents issuing from pending U.S. and foreign applications will have expiration dates of April 2033 and April 2043.

Zoliflodacin

Our intellectual property portfolio for zoliflodacin contains patent applications directed to compositions of matter for zoliflodacin and other chemical analogs, as well as synthetic methods and methods of use and modes of treatment. As of February 15, 2023, we owned seven issued U.S. patents, 74 issued foreign patents as well as two pending foreign patent applications. The issued foreign patents are in several jurisdictions, including Australia, Brazil, Canada, China, Eurasia, the European Union, Hong Kong, India, Israel, Japan, Mexico, New Zealand, Philippines, Singapore, South Africa, South Korea, Taiwan and the United Kingdom. Issued U.S. and foreign patents and patents issuing from pending U.S. and foreign applications have expiration dates of October 2029, January 2034 and May 2035.

Trademarks, Trade Secrets and Know-How

Our trademark portfolio currently consists of various registered trademark and service mark rights in several jurisdictions, including the United States, the European Union, Japan, Argentina, Australia, Brazil, Canada, India, Mexico, Norway, the Russian Federation, South Korea, Switzerland, Taiwan, Turkey and the United Kingdom, and pending applications in other jurisdictions. In connection with the ongoing development and advancement of our products and services in the United States and various international jurisdictions, we routinely seek to create protection for our marks and enhance their value by pursuing trademarks and service marks where available and when appropriate. In addition to patents and trademark protection, we rely upon unpatented trade secrets and know-how and continuing technological innovation to develop and maintain our competitive position. We seek to protect our proprietary information, in part, using confidentiality agreements with our commercial partners, collaborators, employees, and consultants, and invention assignment agreements with our employees. These agreements are designed to protect our proprietary information and, in the case of the invention assignment agreements, to grant us ownership of technologies that are developed through a relationship with a third party. These agreements may be breached, and we may not have adequate remedies for any breach. In addition, our trade secrets may otherwise become known or be independently discovered by competitors. To the extent that our commercial partners, collaborators, employees, and consultants use intellectual property owned by others in their work for us, disputes may arise as to the rights in related or resulting know-how and inventions.

Our Strategic Partnership with Sarissa Capital

Strategic Advisory Agreement

On December 11, 2020, we entered into a Strategic Advisory Agreement (the “Services Agreement”) with Sarissa Capital Management LP (“Sarissa Capital”), pursuant to which Sarissa Capital provides a variety of strategic services to us in order to assist

us in the development and execution of our acquisition strategy intended to diversify our assets and the potential sources of revenue. Sarissa Capital is considered to be a related party due to its investment in Innoviva and its representation on our board of directors.

Partnership Agreement

On December 11, 2020, Innoviva Strategic Partners LLC, our wholly owned subsidiary ("Strategic Partners"), entered into a subscription agreement and an Amended and Restated Limited Partnership Agreement (the "Partnership Agreement") pursuant to which Strategic Partners became a limited partner of ISP Fund LP (the "Partnership"). The general partner of the Partnership is an affiliate of Sarissa Capital and, pursuant to an investment management agreement, Sarissa Capital acts as the investment adviser to the Partnership. Strategic Partners made a $300 million initial contribution to the Partnership. The Partnership was formed for the purposes of investing in equity securities in the healthcare, pharmaceutical and biotechnology industries.

In May 2021, Strategic Partners received a distribution of $110.0 million from the Partnership to provide funding to us for a strategic repurchase of shares held by GSK. Pursuant to the letter agreement entered into between Strategic Partners, the Partnership, and Sarissa Capital Fund GP LP on May 20, 2021, Strategic Partners agreed to make additional capital contributions to the Partnership in an aggregate amount equal to the amount of the May 2021 distribution prior to March 31, 2022. A $110.0 million contribution was made during the first quarter of 2022.

Human Capital

As of December 31, 2022, we had 101 employees, all of whom were full-time employees. None of our employees are represented by a labor union or covered by a collective bargaining agreement, and we consider our relations with our employees to be good. We also hire consultants and contract with third parties, as needed, to provide additional resources to support our business activities.

Our key human capital management objectives are to identify, recruit, integrate, retain and motivate our new and existing employees. We believe that our compensation and benefit programs are appropriately designed to attract and retain qualified talent. Employees receive an annual base salary and are eligible to earn performance-based cash bonuses. To create and maintain a successful work environment, we offer a comprehensive package of additional benefits that support the physical and mental health and wellness of all of our employees and their families and flexible working arrangements. Additionally, we grant equity awards in order to allow employees to share in the performance of the Company. The Chief Executive Officer regularly updates our board of directors and our committees on the operation and status of these human capital trends and activities.

Diversity, Equity and Inclusion

We have created an environment that fosters individual development while maintaining consistency in our corporate values and code of conduct. We offer seminars from external resources on diversity, equity and inclusion, or DEI, best practices and promote the fair treatment and full participation of all people in our workplace.

Health, Safety and Wellness

We strive to provide pay, benefits and other employee services that are competitive to market in the life sciences industry and create incentives to attract and retain employees. Our compensation package includes market-competitive pay, stock options and restrictive stock units, bonuses, employee spot awards, health care and retirement benefits, paid time off and family leave. We utilize third party consultants to review and update our compensation practices annually. We are also committed to the continued development of our people, providing opportunities for employees to further their career development through internal training and education programs and third party online training programs.

Information about our Executive Officers

The following table sets forth the name, age, and position of each of our executive officers as of February 28, 2023:

Name	Age	Positions Held
Pavel Raifeld	39	Chief Executive Officer
Marianne Zhen	54	Chief Accounting Officer

Pavel Raifeld, CFA, was appointed Chief Executive Officer in May 2020. Prior to his appointment, Mr. Raifeld, served on the investment team at Sarissa Capital Management LP. Earlier, he was a senior member of the healthcare investment banking team at Credit Suisse Securities (USA) LLC. Previously, Mr. Raifeld worked as a consultant, primarily specializing in advising biopharmaceutical companies, at McKinsey & Company, Inc. and The Boston Consulting Group Ltd. Mr. Raifeld earned an AB degree from Harvard University and an MBA degree from Columbia University.

Marianne Zhen, CPA, was appointed Chief Accounting Officer in July 2018. Prior to joining Innoviva in October 2014, Ms. Zhen served as the Corporate Controller at Steelwedge Software Inc. from 2012 to 2014, Intelmate from 2011 to 2012 and Model N, Inc. from 2007 to 2011. Previously, Ms. Zhen served as a member of the board of directors of CalCPA Peninsula Silicon Valley Chapter. Ms. Zhen earned a Bachelor of Science degree in Business Administration with a concentration in Accounting from San Francisco State University. She is a member of the American Institute of Certified Public Accountants (AICPA) and a member of the California Society of Certified Public Accountants (CalCPA).

Code of Business Conduct

The Company has adopted the Innoviva, Inc. Code of Business Conduct that applies to all directors, officers and employees. The Code of Business Conduct, as amended through March 9, 2021, is available on the corporate governance section of our website at *www.inva.com*. If the Company makes any substantive amendments to the Code of Business Conduct or grants a waiver from any provision of such code to any executive officer or director, the Company will promptly disclose the nature of the amendment or waiver, as required by applicable law.

Available Information

Our web page address is *www.inva.com*. Our investor relations website is located at *http://investor.inva.com*. We make available free of charge on our investor relations website under "SEC Filings" our Annual Reports on Form 10-K, Quarterly Reports on Form 10-Q, Current Reports on Form 8-K, our directors' and officers' Section 16 Reports and any amendments to those reports after filing or furnishing such materials to the SEC. The information found on our website is not part of this or any other report that we file with or furnish to the SEC. Innoviva and the Innoviva logo are registered trademarks of Innoviva, Inc. Trademarks, tradenames or service marks of other companies appearing in this report are the property of their respective owners.

ITEM 1A. RISK FACTORS

Summary of Risk Factors

The Company is subject to a number of risks that if realized could affect its business, financial condition, results of operations, cash flows and access to liquidity materially. The Company's business is subject to uncertainties and risks including:

- RELVAR®/BREO® ELLIPTA® and ANORO® ELLIPTA® face substantial competition for their intended uses in the targeted markets from products discovered, developed, launched and commercialized both by GSK and by other pharmaceutical companies, which could cause the royalties payable to us pursuant to the GSK Agreements to be less than expected, which in turn would harm our business and cause the price of our securities to fall.

- We are dependent on GSK for the successful commercialization and development of the products developed under the GSK Agreements. If GSK does not devote sufficient resources to the commercialization and development of these products, is unsuccessful in its efforts, or chooses to reprioritize its commercial programs, our business would be materially harmed.

- Our debt including our convertible subordinated notes and convertible senior notes are senior in capital structure and cash flow, respectively, to our common stockholders. Satisfying the obligations relating to our debt could adversely affect our liquidity or the amount or timing of potential distributions to our stockholders.

- GSK has indicated to us that it believes its consent may be required before we can engage in certain royalty monetization transactions with third parties, which may inhibit our ability to engage in these transactions.

- If clinical trials of our product candidates fail to demonstrate safety and efficacy to the satisfaction of the FDA, the EMA or other comparable regulatory authorities, or do not otherwise produce favorable results, we may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of that product candidate.

- We rely on collaborations with third parties for the development of our product candidates, and we may seek additional collaborations in the future. If those collaborations are not successful, we may not be able to capitalize on the market potential of these product candidates.

- Even if any of our product candidates receives marketing approval, such product candidate may fail to achieve the degree of market acceptance by physicians, patients, third-party payors and others in the medical community necessary for commercial success.
- We might not be able to successfully integrate our operations with those of Entasis and/or La Jolla and other assets that we may acquire.
- If we engage in future acquisitions or strategic collaborations, this may increase our capital requirements, dilute our stockholders, cause us to incur debt or assume contingent liabilities and subject us to other risks.
- Even if we complete the necessary preclinical studies and clinical trials, the regulatory approval process is expensive, time-consuming and uncertain and may prevent us or any future collaborators from obtaining approvals for the commercialization of some or all of our product candidates. As a result, we cannot predict when or if, and in which territories, we, or any future collaborators, will obtain marketing approval to commercialize a product candidate.

Risks Related to our Business

Currently, we derive most of our revenues from GSK and our near-term success depends in large part on GSK's ability to successfully develop and commercialize the products in the respiratory programs partnered with GSK.

Pursuant to the GSK Agreements, GSK is responsible for the development and commercialization of products in the partnered respiratory programs. Royalty revenues from RELVAR®/BREO® ELLIPTA® and ANORO® ELLIPTA® are expected to represent the majority of our foreseeable future revenues from GSK. The amount and timing of revenue from such royalties are unknown and highly uncertain. Our near-term success depends in large part upon the performance by GSK of its commercial obligations under the GSK Agreements and the commercial success of RELVAR®/BREO® ELLIPTA® and ANORO® ELLIPTA®. We have no control over GSK's marketing and sales efforts, and GSK might not be successful, which would harm our business and cause the price of our securities to fall.

Our quarterly royalty revenues may fluctuate due to a variety of factors, many of which are outside of our control. The amount of royalties and milestone payments, if any, we receive will depend on many factors, including the following:

- the extent and effectiveness of the sales and marketing and distribution support GSK provides to our partnered products;
- market acceptance and demand for our partnered products;
- changes in the treatment paradigm or standard of care for COPD or asthma, for instance through changes to the GOLD (Global Initiative for Chronic Obstructive Lung Disease) guidelines;
- the competitive landscape of generic and branded products and developing therapies that compete with our products owned by GSK (such as Advair®) but which are not partnered with us and pricing pressure in the respiratory markets targeted by our partnered products;
- the size of the market for our partnered products;
- the mix of sales of our partnered products;
- decisions as to the timing of product launches, pricing and discounts;
- reprioritization of GSK's commercial efforts on other products owned by GSK (such as Advair®), which are not partnered with us;
- GSK's ability to expand the indications for which our partnered products can be marketed;
- a satisfactory efficacy and safety profile as demonstrated in a broad patient population;
- acceptance of, and ongoing satisfaction with, our partnered products by the medical community, patients receiving therapy and third-party payors;
- timing and amounts of payor rebate adjustments and prior period rebate adjustments;

- seasonal fluctuations of demand;
- the ability of patients to be able to afford our partnered products or obtain health care coverage that covers our partnered products;
- safety concerns in the marketplace for respiratory therapies in general and with our partnered products in particular;
- regulatory developments relating to the manufacture or continued use of our partnered products;
- the requirement to conduct additional post-approval studies or trials for our partnered products;
- GSK's ability to obtain regulatory approval of our partnered products in additional countries;
- the unfavorable outcome of any potential litigation relating to our partnered products;
- general economic conditions in the jurisdictions where our partnered products are sold, including microeconomic disruptions or slowdowns; or
- if our royalty revenue or operating results fall below the expectations of investors or securities analysts or below any guidance we may provide to the market, the price of our common stock could decline substantially.

When the FDA or other applicable regulatory authorities approve generic products, including but not limited to generic forms of Advair, that compete with RELVAR®/BREO® ELLIPTA®, and ANORO® ELLIPTA® or a generic form of RELVAR®/BREO® ELLIPTA®, the royalties payable to us pursuant to the GSK Agreements will be less than anticipated, which in turn would harm our business and the price of our securities could fall.

Once an NDA or marketing authorization application outside the United States is approved, the product covered thereby becomes a "listed drug" that can, in turn, be cited by potential competitors in support of approval of an ANDA in the United States. Agency regulations and other applicable regulations and policies provide incentives to manufacturers to create modified, non-infringing versions of a drug to facilitate the approval of an ANDA or other application for generic substitutes in the United States and in nearly every pharmaceutical market around the world. Numerous companies have brought to market generic forms of the ICS/LABA drug Advair® since certain patents covering the Advair® delivery device expired in 2016. In general, these manufactures are required to conduct a number of clinical efficacy, pharmacokinetic and device studies to demonstrate equivalence to Advair, per FDA's September 2013 draft guidance document. These studies are designed to demonstrate that the generic product has the same active ingredient(s), dosage form, strength, exposure and clinical efficacy as the branded product. These generic equivalents, which must meet the same exacting quality standards as branded products, may be significantly less costly to bring to market, and companies that produce generic equivalents are generally able to offer their products at lower prices. Thus, after the introduction of a generic competitor, a significant percentage of the sales of any branded product and products that may compete with such branded product is typically lost to the generic product.

In January 2019, Mylan announced that the FDA approved Wixela™ Inhu™ (fluticasone propionate and salmeterol inhalation powder, USP), the first generic of ADVAIR DISKUS®. In that same month, Teva announced that the FDA approved two of their products for adolescent and adult patients with asthma, one of which is AirDuo™ RespiClick® (fluticasone propionate and salmeterol inhalation powder), a non-AB substitutable generic version of Advair®. In January 2020, Astra Zeneca launched an authorized generic version of Symbicort. In December 2020, Hikma/Vectura announced that it received FDA approval and launched its generic version of GSK's Advair Diskus®.

In April 2016, the FDA issued draft guidance documents covering Fluticasone Furoate/Vilanterol Trifenatate (FF/VI), the active ingredients used in RELVAR®/BREO® ELLIPTA®. Introduction of generic products that compete against ICS/LABA products, like RELVAR®/BREO® ELLIPTA®, would materially adversely impact our future royalty revenue, profitability and cash flows. We cannot yet ascertain what impact these generic products and any future approved generic products will have on any sales of RELVAR®/BREO® ELLIPTA® or ANORO® ELLIPTA®, if approved.

Reduced prices and reimbursement rates due to the actions of governments, payors, or competition or other healthcare cost containment initiatives such as restrictions on use, may negatively impact royalties generated under the GSK Agreements.

The continuing efforts of governments, pharmaceutical benefit management organizations ("PBMs"), insurance companies, managed care organizations and other payors of health care costs to contain or reduce costs of health care has adversely affected the price, market access, and total revenues of RELVAR®/BREO® ELLIPTA®, and ANORO® ELLIPTA® and may continue to adversely

affect them in the future. In addition, we have experienced and expect to continue to experience increased competitive activity, which has resulted in lower overall prices for our products.

The Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010 (together, "PPACA") and other legislative or regulatory requirements or potential legislative or regulatory actions regarding healthcare and insurance matters, along with the trend toward managed healthcare in the U.S., could adversely influence the purchase of healthcare products and reduce demand and prices for our partnered products. This could harm GSK's ability to market our partnered products and significantly reduce future revenues. For example, when GSK launched RELVAR®/BREO® ELLIPTA® for the treatment of COPD in the U.S. in October 2013, GSK experienced significant challenges gaining coverage at some of the largest PBMs, healthcare payors, and providers and lower overall prices than expected. Recent actions by U.S. PBMs in particular have increased discount levels for respiratory products resulting in lower net sales pricing realized for products in our collaboration. In addition, in certain foreign markets, the pricing of prescription drugs is subject to government control and reimbursement may in some cases be unavailable. We believe that pricing pressures will continue and may increase. This may make it difficult for GSK to sell our partnered products at a price acceptable to us or GSK or to generate revenues in line with our analysts' or investors' expectations, which may cause the price of our securities to fall.

More recently, presidential administrations and the U.S. Congress have taken actions in an effort to modify or replace PPACA and to implement or pass other reforms to the healthcare system, including proposed legislation related to the pricing of pharmaceuticals. There is uncertainty with respect to any potential changes that may be proposed and what the impact, if any, will be on our business, including the impact on coverage and reimbursement for healthcare items and services covered by plans that were authorized by PPACA. However, we cannot predict the ultimate content, timing or effect of any healthcare reform legislation or the impact of potential legislation on us.

We expect that additional state and federal healthcare reform measures will be considered and potentially adopted, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our products once approved or additional pricing pressures and may adversely affect our operating results.

A portion of our current revenues are from royalties derived from sales of our respiratory products partnered with GSK, RELVAR®/BREO® ELLIPTA® and ANORO® ELLIPTA®. If the treatment paradigm for the indications our partnered products are approved for change or if GSK is unable to, or does not devote sufficient resources to, maintain or continue increasing sales of these products, our results of operations will be adversely affected.

We currently depend, in part, on royalties from sales of our products partnered with GSK to support our existing operations. The treatment paradigm for COPD and asthma constantly evolves. For instance, in November 2018, the GOLD guidelines were revised to favorably position bronchodilator monotherapy and LABA/LAMA treatment ahead of ICS/LABA for the treatment of COPD unless the patient has frequent exacerbations, or an eosinophil count greater than 300 per cubic microliter. The use of ICS in COPD is also recommended for patients requiring triple therapy (LABA, LAMA, ICS). If the treatment paradigms were to change further, causing our partnered products to fall out of favor, or if GSK were unable, or did not devote sufficient resources, to maintain or continue increasing RELVAR®/BREO® ELLIPTA® and ANORO® ELLIPTA® sales, our results of operations would likely suffer, and the price of our securities could fall.

If the commercialization of RELVAR®/BREO® ELLIPTA® and ANORO® ELLIPTA® in the countries in which they have received regulatory approval encounters any delays or adverse developments, or perceived delays or adverse developments, or if sales or payor coverage does not meet investors', analysts', or our expectations, our business will be harmed, and the price of our securities could fall.

Under our agreements with our collaborative partner GSK, GSK has full responsibility for commercialization of RELVAR®/BREO® ELLIPTA® and ANORO® ELLIPTA®. GSK has launched RELVAR®/BREO® ELLIPTA® and ANORO® ELLIPTA® in a number of countries, including the United States, Canada, Japan, the United Kingdom, and Germany, among others. The commercialization of the products in countries where they are already launched and the commercialization launch in new countries are still subject to fluctuating overall pricing levels and uncertain timeframes to obtain payor coverage. Any delays or adverse developments or perceived additional delays or adverse developments with respect to the commercialization of RELVAR®/BREO® ELLIPTA® and ANORO® ELLIPTA® including if sales or payor coverage does not meet investors', analysts', or our expectations, would significantly harm our business and the price of our securities could fall.

We are dependent on GSK for the successful commercialization and development of products under the GSK Agreements. If GSK does not devote sufficient resources to the commercialization or development of these products, is unsuccessful in its efforts, or chooses to reprioritize its commercial programs, our business would be materially harmed.

GSK is responsible for all clinical and other product development, regulatory, manufacturing and commercialization activities for products developed under the GSK Agreements, including RELVAR®/BREO® ELLIPTA® and ANORO® ELLIPTA®. Our royalty revenues under the GSK Agreements may not meet our, analysts', or investors' expectations, due to a number of important factors. GSK has a substantial respiratory product portfolio in addition to the partnered products that are covered by the GSK Agreements. GSK may make respiratory product portfolio decisions or statements about its portfolio which may be, or may be perceived to be, harmful to the respiratory products partnered with us. For instance, GSK has wide discretion in determining the efforts and resources that it will apply to the development and commercialization of our partnered products. In addition, GSK may determine to focus its commercialization efforts on its own products. For example, in January 2015, GSK launched Incruse® (UMEC) in the U.S., which is a LAMA for the treatment of COPD. GSK may determine to focus its marketing efforts on Incruse, which could have the effect of decreasing the potential market share of ANORO® ELLIPTA® and lowering the royalties we may receive for such product. Alternatively, GSK may decide to market to eventually compete directly against sales of RELVAR®/BREO® ELLIPTA®. In the event GSK does not devote sufficient resources to the commercialization of our partnered products or chooses to reprioritize its commercial programs, our business, operations and stock price would be negatively affected.

Any adverse change in FDA policy or guidance regarding the use of LABAs to treat asthma could significantly harm our royalty revenues and the price of our securities could fall.

On February 18, 2010, the FDA announced that LABAs should not be used alone in the treatment of asthma and it will require manufacturers to include this warning in the product labels of these drugs, along with taking other steps to reduce the overall use of these medicines. The FDA now requires that the product labels for LABA medicines reflect, among other things, that the use of LABAs is contraindicated without the use of an asthma controller medication such as an inhaled corticosteroid, that LABAs should only be used long term in patients whose asthma cannot be adequately controlled on asthma controller medications, and that LABAs should be used for the shortest duration of time required to achieve control of asthma symptoms and discontinued, if possible, once asthma control is achieved. In addition, in March 2010, the FDA held an Advisory Committee to discuss the design of medical research studies (known as "clinical trial design") to evaluate serious asthma outcomes (such as hospitalizations, a procedure using a breathing tube known as intubation, or death) with the use of LABAs in the treatment of asthma in adults, adolescents, and children. Further, in April 2011, the FDA announced that to further evaluate the safety of LABAs, it required the manufacturers of currently marketed LABAs to conduct additional randomized, double blind, controlled clinical trials comparing the addition of LABAs to inhaled corticosteroids versus inhaled corticosteroids alone. These post-marketing studies have been completed and the FDA stated that treating asthma with LABAs in combination with ICS did not result in significantly more serious asthma-related side effects than treatment with ICS alone. The FDA subsequently removed the black box warning from the ICS/LABA package inserts. Although this concern appears to be resolved, it is unknown at this time what, if any, future concerns could impact the use of ICS/LABA and its potential impact on the prospects for FF/VI. Any adverse change in FDA policy or guidance regarding the use of LABAs to treat asthma could significantly harm our business and the price of our securities could fall.

Any adverse developments to the regulatory status of either RELVAR®/BREO® ELLIPTA® or ANORO® ELLIPTA® in the countries in which they have received regulatory approval, including labeling restrictions, safety findings, or any other limitation to usage, would harm our business and may cause the price of our securities to fall.

Although RELVAR®/BREO® ELLIPTA® and ANORO® ELLIPTA® are approved and marketed in a number of countries, it is possible that adverse changes to the regulatory status of these products could occur in the event new safety issues are identified, treatment guidelines are changed, or new studies fail to demonstrate product benefits. A number of notable pharmaceutical products have experienced adverse developments during commercialization that have resulted in the product being withdrawn, approved uses being limited, or new warnings being included. In the event that any adverse regulatory changes were to occur to any of our products, our business would be harmed, and the price of our securities could fall.

Any adverse developments or results or perceived adverse developments or results with respect to the ongoing studies for FF/VI in asthma or COPD, for UMEC/VI in COPD, or any future studies would significantly harm our business and the price of our securities could fall, and if regulatory authorities in those countries in which approval has not yet been granted determine that the ongoing studies for FF/VI in asthma or COPD or the ongoing studies for UMEC/VI for COPD do not demonstrate adequate safety and efficacy, the continued development of FF/VI or UMEC/VI or both could be significantly delayed, they might not be approved by these regulatory authorities, and even if approved they may be subject to restrictive labeling, any of which might harm our business, and the price of our securities could fall.

Although we have announced the completion of, and reported certain top-line data from, the Phase 3 registrational program for FF/VI in COPD and asthma, additional studies of FF/VI are underway or may commence in the future. Any adverse developments or perceived adverse developments with respect to any prior, current or future studies in these programs could significantly harm our business and the price of our securities could fall.

Although the FDA, the European Medicines Agency, the Japanese Ministry of Health, Labour and Welfare and Health Canada and other jurisdictions have approved ANORO® ELLIPTA®, it has not yet been approved in all jurisdictions.

Any adverse developments or results or perceived adverse developments or results with respect to other pending or future regulatory submissions for the FF/VI program or the UMEC/VI program might significantly harm our business and the price of our securities could fall. Examples of such adverse developments include, but are not limited to:

- not every study, nor every dose in every study, in the Phase 3 programs for FF/VI achieved its primary endpoint and regulatory authorities may determine that additional clinical studies are required;
- safety, efficacy or other concerns arising from clinical or non-clinical studies in these programs having to do with the LABA VI, which is a component of FF/VI and UMEC/VI;
- analysts adjusting their sales forecasts downward from previous projections based on results or interpretations of results of prior, current or future studies;
- safety, efficacy or other concerns arising from clinical or non-clinical studies in these programs;
- regulatory authorities determining that the Phase 3 programs in asthma or in COPD raise safety concerns or do not demonstrate adequate efficacy; or
- any change in FDA (or comparable foreign regulatory agency) policy or guidance regarding the use of LABAs to treat asthma or the use of LABAs combined with a LAMA to treat COPD.

RELVAR®/BREO® ELLIPTA® and ANORO® ELLIPTA® face substantial competition for their intended uses in the targeted markets from products discovered, developed, launched and commercialized both by GSK and by other pharmaceutical companies, which could cause the royalties payable to us pursuant to the LABA Collaboration Agreement to be less than expected, which in turn would harm our business and cause the price of our securities to fall.

GSK has responsibility for obtaining regulatory approval, launching and commercializing RELVAR®/BREO® ELLIPTA®, and ANORO® ELLIPTA® for their intended uses in the targeted markets around the world. While these products have received regulatory approval and have been launched and commercialized in the U.S. and certain other targeted markets, the products face substantial competition from existing products previously developed and commercialized both by GSK and by other competing pharmaceutical companies and can expect to face additional competition from new products that are discovered, developed and commercialized by the same pharmaceutical companies and other competitors going forward. For example, sales of generic Advair®, GSK's approved medicine for both COPD and asthma, continue to have a negative impact on sales of RELVAR®/BREO® ELLIPTA®.

Many of the pharmaceutical companies competing in respiratory markets are international in scope with substantial financial, technical and personnel resources that permit them to discover, develop, obtain regulatory approval and commercialize new products in a highly efficient and low-cost manner at competitive prices to consumers. In addition, many of these competitors have substantial commercial infrastructure that facilitates commercializing their products in a highly efficient and low-cost manner at competitive prices to consumers. The market for products developed for treatment of COPD and asthma continues to experience significant innovation and reduced cost in bringing products to market over time. There can be no assurance that RELVAR®/BREO® ELLIPTA® and ANORO® ELLIPTA® will not be replaced by new products that are deemed more effective at lower cost to consumers. The ability of RELVAR®/BREO® ELLIPTA®, and ANORO® ELLIPTA® to succeed and achieve the anticipated level of sales depends on the

commercial and development performance of GSK to achieve and maintain a competitive advantage over other products with the same intended use in the targeted markets.

If sales of RELVAR®/BREO® ELLIPTA® and ANORO® ELLIPTA® are less than anticipated because of existing or future competition in the markets in which they are commercialized, including competition from existing and new products that are perceived as lower cost or more effective, our royalty payments could be less than anticipated, which in turn would harm our business and cause the price of our securities to fall.

We may not be able to utilize all of our net operating loss carryforwards.

We have net operating loss carryforwards and other significant U.S. tax attributes that we believe could offset otherwise taxable income in the U.S. As a part of the overall Spin-Off transaction, the transfer of certain assets by us to Theravance Biopharma and our distribution of Theravance Biopharma ordinary shares resulted in taxable transfers pursuant to applicable provisions of the Internal Revenue Code of 1986, as amended (the "Code") and Treasury Regulations. The taxable gain recognized by us attributable to the transfer of certain assets to Theravance Biopharma generally equaled the excess of the fair market value of each asset transferred over our adjusted tax basis in such asset. Although we did not recognize any gain with respect to the cash we transferred to Theravance Biopharma, we may recognize substantial gain based on the fair market value of the other assets (other than cash) transferred to Theravance Biopharma. The determination of the fair market value of these assets is subjective and could be subject to adjustments or future challenge by the Internal Revenue Service ("IRS"), which could result in an increase in the amount of gain realized by us as a result of the transfer. Our U.S. federal income tax resulting from any gain recognized upon the transfer of our assets to Theravance Biopharma (including any increased U.S. federal income tax that may result from a subsequent determination of higher fair market values for the transferred assets), may be reduced by our net operating loss carryforward. The net operating loss carryforwards available in any year to offset our net taxable income will be reduced following a more than 50% change in ownership during any period of 36 consecutive months (an "ownership change") as determined under the Code. Transactions involving our common stock, even those outside our control, such as purchases or sales by investors, within the testing period could result in an ownership change. We have conducted an analysis to determine whether an ownership change had occurred since inception through December 31, 2022 and concluded that it is more likely than not that the Company did not experience an ownership change during the testing period. Subsequent changes in our ownership or sale of our stock could have the effect of limiting the use of our net operating losses in the future. There may be certain annual limitations for utilization based on the above-described ownership change provisions. In addition, we may not be able to have sufficient future taxable income prior to their expiration because net operating losses have carryforward periods. Future changes in federal and state tax laws pertaining to net operating loss carryforwards may also cause limitations or restrictions from us claiming such net operating losses. If the net operating loss carryforwards become unavailable to us or are fully utilized, our future taxable income will not be shielded from federal and state income taxation absent certain U.S. federal and state tax credits, and the funds otherwise available for general corporate purposes would be reduced.

If any product candidates in any respiratory program partnered with GSK were not approved by regulatory authorities or are determined to be unsafe or ineffective in humans, our business would be adversely affected and the price of our securities could fall.

The FDA must approve any new medicine before it can be marketed and sold in the U.S. Our partner GSK must provide the FDA and similar foreign regulatory authorities with data from preclinical and clinical studies that demonstrate that the product candidates are safe and effective for a defined indication before they can be approved for commercial distribution. GSK will not obtain this approval for a partnered product candidate unless and until the FDA approves an NDA. The processes by which regulatory approvals are obtained from the FDA to market and sell a new product are complex, require a number of years and involve the expenditure of substantial resources. In order to market medicines in foreign countries, separate regulatory approvals must be obtained in each country. The approval procedure varies among countries and can involve additional testing, and the time required to obtain approval may differ from that required to obtain FDA approval. Approval by the FDA does not ensure approval by regulatory authorities in other countries, and approval by one foreign regulatory authority does not ensure approval by regulatory authorities in other foreign countries or by the FDA. Conversely, failure to obtain approval in one or more country may make approval in other countries more difficult.

Clinical studies involving product candidates partnered with GSK may reveal that those candidates are ineffective, inferior to existing approved medicines, unacceptably toxic, or that they have other unacceptable side effects. In addition, the results of preclinical studies do not necessarily predict clinical success, and larger and later-stage clinical studies may not produce the same results as earlier-stage clinical studies.

Frequently, product candidates that have shown promising results in early preclinical or clinical studies have subsequently suffered significant setbacks or failed in later clinical or non-clinical studies. In addition, clinical and non-clinical studies of potential products often reveal that it is not possible or practical to continue development efforts for these product candidates. If these studies

are substantially delayed or fail to prove the safety and effectiveness of product candidates in development partnered with GSK, GSK may not receive regulatory approval for such product candidates and our business and financial condition could be materially harmed and the price of our securities might fall.

Several well-publicized Complete Response letters issued by the FDA and safety-related product withdrawals, suspensions, post-approval labeling revisions to include boxed warnings and changes in approved indications over the last several years, as well as growing public and governmental scrutiny of safety issues, have created a conservative regulatory environment. The implementation of new laws and regulations and revisions to FDA clinical trial design guidance have increased uncertainty regarding the approvability of a new drug. Further, there are additional requirements for approval of new drugs, including advisory committee meetings for new chemical entities, and formal risk evaluation and mitigation strategy at the FDA's discretion. These laws, regulations, additional requirements and changes in interpretation could cause non-approval or further delays in the FDA's review and approval of any product candidates in any respiratory program partnered with GSK.

Even if product candidates in any respiratory program partnered with GSK receive regulatory approval, as is the case with RELVAR®/BREO® ELLIPTA® and ANORO® ELLIPTA®, commercialization of such products may be adversely affected by regulatory actions and oversight.

Even if GSK receives regulatory approval for product candidates in any respiratory program partnered with GSK, this approval may include limitations on the indicated uses for which GSK can market the medicines or the patient population that may utilize the medicines, which may limit the market for the medicines or put GSK at a competitive disadvantage relative to alternative therapies. These restrictions make it more difficult to market the approved products.

For example, at the joint meeting of the Pulmonary-Allergy Drugs Advisory Committee and Drug Safety and Risk Management Advisory Committee of the FDA regarding the sNDA for BREO® ELLIPTA® as a treatment for asthma, the advisory committee recommended that a large LABA safety trial with BREO® ELLIPTA® should be required in adults and in children ages 12-17, similar to the ongoing LABA safety trials being conducted as an FDA Post-Marketing Requirement by each of the manufacturers of LABA containing asthma treatments. The FDA did not concur with the recommendation. A pediatric program including patients 5-17 years of age is currently ongoing.

In addition, the manufacturing, labeling, packaging, adverse event reporting, advertising, promotion and recordkeeping for the approved product remain subject to extensive and ongoing regulatory requirements. If we or GSK become aware of previously unknown problems with an approved product in the U.S. or overseas or at contract manufacturers' facilities, a regulatory authority may impose restrictions on the product, the contract manufacturers or on GSK, including requiring it to reformulate the product, conduct additional clinical studies, change the labeling of the product, withdraw the product from the market or require the contract manufacturer to implement changes to its facilities. GSK is also subject to regulation by regional, national, state and local agencies, including the Department of Justice, the Federal Trade Commission, the Office of Inspector General of the U.S. Department of Health and Human Services and other regulatory bodies, as well as governmental authorities in those foreign countries in which any of the product candidates in any respiratory program partnered with GSK are approved for commercialization. The Federal Food, Drug, and Cosmetic Act, the Public Health Service Act and other federal and state statutes and regulations govern to varying degrees the research, development, manufacturing and commercial activities relating to prescription pharmaceutical products, including non-clinical and clinical testing, approval, production, labeling, sale, distribution, import, export, post-market surveillance, advertising, dissemination of information and promotion. Any failure to maintain regulatory approval would limit GSK's ability to commercialize the product candidates in any respiratory program partnered with GSK, which could materially and adversely affect our business and financial condition, and which may cause the price of our securities to fall.

Acquisitions or strategic investments we have made or may make could turn out to be unsuccessful.

As part of our strategy, we frequently monitor and analyze acquisition or investment opportunities that we believe will create value for our shareholders.

Existing or future acquisitions and investments could involve numerous risks that may prevent us from fully realizing the benefits that we anticipated as a result of the transaction. These risks include the failure to derive any commercial value from the acquired technology, products and intellectual property including as a result of the failure to obtain regulatory approval or to monetize products once approved, as well as risks from lengthy product development and high upfront development costs without guarantee of successful results. Patents and other intellectual property rights covering acquired technology and/or intellectual property may not be obtained, and if obtained, may not be sufficient to fully protect the technology or intellectual property. We may be subject to liabilities, including unanticipated litigation costs, that are not covered by indemnification protection we may obtain. As we pursue or consummate a strategic acquisition or investment, we may value the acquired or funded company incorrectly, fail to successfully manage our operations as our asset diversity increases, expend unforeseen costs during the acquisition or integration process, or

encounter other unanticipated risks or challenges. Once an investment is made, we may fail to value it accurately, properly account for it in our consolidated financial statements, or successfully divest it or otherwise realize the value which we originally invested or have subsequently reflected in our consolidated financial statements. Any failure by us to effectively limit such risks as we implement our acquisitions or strategic investments could have a material adverse effect on our business, financial condition or results of operations and may negatively impact our net income and cause the price of our securities to fall.

We have a significant amount of debt including our convertible subordinated notes and convertible senior notes that are senior in capital structure and cash flow, respectively, to our common stockholders. Satisfying the obligations relating to our debt could adversely affect our liquidity or the amount or timing of potential distributions to our stockholders.

As of December 31, 2022, we had $549.7 million in total debt outstanding, comprised primarily of $96.2 million in principal that remains outstanding under our convertible subordinated notes due 2023 (the "2023 Notes"), $192.5 million in principal outstanding under our convertible senior notes due 2025 (the "2025 Notes") and $261.0 million in principal outstanding under our convertible notes due 2028 (the "2028 Notes") (the 2023 Notes, 2025 Notes and 2028 Notes, hereinafter, the "Notes"). The Notes are unsecured debt and, with the exception of the 2028 Notes, are not redeemable by us prior to the maturity date. Holders of the Notes may require us to purchase all or any portion of their Notes at 100% of their principal amount, plus any unpaid interest, upon a fundamental change. A fundamental change is generally defined to include a merger involving us, an acquisition of a majority of our outstanding common stock, and, under the 2023 Notes, the change of a majority of our board of directors without the approval of the board of directors. In addition, to the extent we pursue and complete a monetization transaction or a transaction that modifies our corporate structure, the structure of such transaction may qualify as a fundamental change under the Notes, which could trigger the put rights of the holders of the Notes, in which case we would be required to use a portion of the net proceeds from such transaction to repurchase any Notes put to us.

Satisfying the obligations of this debt could adversely affect the amount or timing of any distributions to our stockholders. We may choose to satisfy, repurchase, or refinance this debt through public or private equity or debt financings if we deem such financings available on favorable terms. If any or all of the Notes are not converted into shares of our common stock before the maturity date, we will have to pay the holders the full aggregate principal amount of the Notes then outstanding. Any of the above payments could have a material adverse effect on our cash position. If we fail to satisfy these obligations, it may result in a default under the indenture, which could result in a default under certain of our other debt instruments, if any. Any such default would harm our business and the price of our securities could fall.

If we lose key management personnel, or if we fail to retain our key employees, our ability to manage our business may be impaired.

Our performance is substantially dependent on the continued service and performance of our management team, who have extensive experience and specialized expertise in our business. None of our employees have employment commitments for any fixed period of time and all may leave our employment at will. If we fail to retain our qualified personnel or to replace them when they leave, our ability to manage our business may be impaired, which may cause the price of our securities to fall.

Prolonged economic uncertainties or downturns, as well as unstable market, credit and financial conditions, may exacerbate certain risks affecting our business and have serious adverse consequences on our business.

The global economic downturn and market instability has made the business climate more volatile and more costly. These economic conditions, and uncertainty as to the general direction of the macroeconomic environment, are beyond our control and may make any necessary debt or equity financing more difficult, more costly, and more dilutive. While we believe we have adequate capital resources to meet current working capital and capital expenditure requirements, a lingering economic downturn or significant increase in our expenses could require additional financing at less than attractive rates or on terms that are excessively dilutive to existing stockholders. Failure to secure any necessary financing in a timely manner and on favorable terms could have a material adverse effect on our stock price and could require us to delay or abandon clinical development plans.

Sales of our partnered products will be dependent, in large part, on reimbursement from government health administration authorities, private health insurers, distribution partners and other organizations. As a result of negative trends in the general economy in the U.S. or other jurisdictions in which we may do business, these organizations may be unable to satisfy their reimbursement obligations or may delay payment. In addition, federal and state health authorities may reduce Medicare and Medicaid reimbursements, and private insurers may increase their scrutiny of claims. A reduction in the availability or extent of reimbursement could negatively affect our or our partners' product sales and revenue.

In addition, we rely on third parties for several important aspects of our business. During challenging and uncertain economic times and in tight credit markets, there may be a disruption or delay in the performance of our third-party contractors, suppliers or

partners. If such third parties are unable to satisfy their commitments to us, our business and results of operations would be adversely affected.

Our success in preclinical studies or clinical trials may not be indicative of results in current or future clinical trials.

Our success in preclinical testing and early clinical trials does not ensure that later clinical trials will generate the same results or otherwise provide adequate data to demonstrate the efficacy and safety of a product candidate. Certain product candidates may fail to show the necessary safety and efficacy in clinical development despite positive results in preclinical studies or having successfully advanced through initial clinical trials.

In addition, the design of a clinical trial can determine whether its results will support approval of a product, and flaws in the design of a clinical trial may not become apparent until the clinical trial is well advanced. We have limited experience designing clinical trials and may be unable to design and execute a clinical trial to support regulatory approval. There is a high failure rate for drugs and biologic products proceeding through clinical trials. Many companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late-stage clinical trials even after achieving promising results in preclinical testing and earlier-stage clinical trials. Data obtained from preclinical and clinical activities are subject to varying interpretations, which may delay, limit or prevent regulatory approval. In addition, we may experience regulatory delays or rejections because of many factors, including changes in regulatory policy during the period of our product candidate development. Any such delays could negatively impact our business, financial condition, results of operations and prospects.

If clinical trials of our product candidates fail to demonstrate safety and efficacy to the satisfaction of the FDA, the EMA or other comparable regulatory authorities, or do not otherwise produce favorable results, we may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of that product candidate.

We, or our potential collaborators, may not commercialize, market, promote, or sell any product candidate without obtaining marketing approval from the FDA, the EMA or other comparable regulatory authority, and we may never receive such approvals. Even if our product candidates appear sufficiently effective and/or safe in patients in well-controlled clinical trials, it is impossible to predict if or when these product candidates will receive regulatory approval. Before obtaining marketing approval from regulatory authorities for the sale of any product candidate, we must complete preclinical development and then conduct extensive clinical trials to demonstrate the safety and efficacy of our product candidates in humans. Clinical testing is expensive, difficult to design and implement, can take many years to complete and is uncertain as to outcome. A failure of one or more clinical trials can occur at any stage of testing. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval of their products.

We may experience numerous unforeseen events prior to, during, or because of, clinical trials that could delay or prevent our ability to receive marketing approval or commercialize our product candidates, including:

- the FDA, the EMA or other comparable regulatory authority may change from the views they have expressed to us as to the design, implementation, and/or interpretation of our clinical trials;
- the FDA may withdraw Fast Track designation if it believes that the designation is no longer supported by data from our clinical development program;
- regulators or institutional review boards may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- we may not reach agreement on acceptable terms with prospective contract research organizations, or CROs, and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and clinical trial sites;
- clinical trials of product candidates may produce negative or inconclusive results;
- we may decide, or regulators may require us, to conduct additional clinical trials or abandon product development programs;
- we may not be able to complete our clinical trials in a timely manner, if at all, for example because the number of patients required for clinical trials of our product candidates may be larger than we anticipate;

- enrollment in these clinical trials may be slower than we anticipate, participants may drop out of these clinical trials at a higher rate than we anticipate, or we may fail to recruit suitable patients to participate in a trial;
- we may fail to comply with regulatory requirements applicable to them, to the FDA's or other comparable regulatory authority's, satisfaction;
- third-party contractors may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all;
- regulators may issue a clinical hold, or regulators or institutional review boards may require that we or our investigators suspend or terminate clinical research for various reasons, including noncompliance with regulatory requirements or a finding that the participants are being exposed to unacceptable health risks;
- the cost of clinical trials of our product candidates may be greater than we anticipate;
- the FDA, the EMA or other comparable regulatory authorities may fail to approve the manufacturing processes or facilities of third-party manufacturers with whom we enter into agreements for clinical and commercial supplies;
- the supply or quality of our product candidates or other materials necessary to conduct clinical trials of our product candidates may be insufficient or inadequate;
- our product candidates, once exposed to greater numbers of patients, may have undesirable side effects or other unexpected characteristics, causing us or our investigators, regulators or institutional review boards to suspend or terminate the clinical trials or cause regulatory authorities to refuse to approve our product candidates or approve them only with significant restrictions on distribution or use;
- even if our clinical trials are successful, the FDA, the EMA or other comparable regulatory authorities may determine that the overall risk-benefit profiles of our product candidates are insufficient to support marketing authorization; and
- the approval policies or regulations of the FDA, the EMA or other comparable regulatory authorities may significantly change in a manner rendering our clinical data insufficient for approval.

If we are required to conduct additional clinical trials or other testing of our product candidates beyond those that we currently contemplate, if we are unable to successfully complete clinical trials or other testing of those product candidates, or if the results of these trials or tests are not positive or are only modestly positive or if there are safety concerns, we may:

- be delayed in obtaining marketing approval for our product candidates;
- not obtain marketing approval at all;
- obtain approval for indications or patient populations that are not as broad as intended or desired;
- obtain approval with labeling that includes significant use or distribution restrictions or safety warnings, such as black box warnings or a REMS program;
- be subject to additional post-marketing testing requirements; or
- be required to remove the product from the market after obtaining marketing approval.

Our product development costs may also increase if we experience delays in testing and we may be required to obtain additional funds to complete clinical trials. We do not know whether any of our preclinical studies or clinical trials will begin as planned, will need to be restructured or will be completed on schedule, or at all. Significant preclinical study or clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize our product candidates or allow our competitors to bring products to market before we do and impair our ability to successfully commercialize our product candidates. In addition, many of the factors that cause, or lead to, delays of clinical trials may ultimately lead to the denial of regulatory approval of a product candidate.

If we are not successful in discovering, developing, and commercializing additional product candidates, our ability to expand and achieve our strategic objectives would be impaired.

Although a substantial amount of our effort will focus on the continued clinical testing and potential regulatory approval of our product candidates, an element of our strategy is to develop and commercialize, either by ourselves or with a collaborator, our product candidates and discover and develop novel product candidates in other therapeutic areas. We are seeking to do so by utilizing our discovery research experience and capabilities to design active new compounds that target causative mechanisms of disease. Research efforts to identify and develop product candidates require substantial technical, financial and human resources, whether or not any product candidates are ultimately identified. Our research programs may initially show promise in identifying potential product candidates, yet fail to yield product candidates for clinical development for many reasons, including the following:

- the research methodology used may not be successful in identifying potential product candidates;
- competitors may develop alternatives that render our product candidates obsolete or less attractive;
- product candidates we develop may nevertheless be covered by third parties' patents or other exclusive rights;
- a product candidate may on further study be shown to have harmful side effects or other characteristics that indicate it is unlikely to be effective or otherwise does not meet applicable regulatory criteria;
- a product candidate may not be capable of being produced in commercial quantities at an acceptable cost, or at all;
- a product candidate may not be accepted as safe and effective by patients, the medical community or third-party payors, if applicable; and
- the FDA, the EMA or other regulatory authorities may not approve or agree with the intended use of a new product candidate.

If we fail to develop and successfully generate revenue from other current and future product candidates, our future prospects may be harmed, and we will be more vulnerable to any problems that we or potential collaborators may encounter in developing and commercializing our current product candidates.

If we or our collaborators experience delays or difficulties in the enrollment of patients in clinical trials, our receipt of necessary regulatory approvals could be delayed or prevented.

We may not be able to initiate, continue or complete clinical trials of our product candidates that we develop if we and our collaborators are unable to locate and enroll a sufficient number of eligible patients to participate in these trials as required by the FDA, the EMA or other comparable regulatory authority. We have limited experience enrolling patients in our clinical trials and cannot predict how successful we will be in enrolling patients in future clinical trials.

For instance, patients involved in our clinical trials are often in the hospital setting and the decision to participate can be made by the caregiver or doctor. Accordingly, seeking consent for patient participation may become difficult when the family and/or the patient may not be available to consider participation in a clinical trial and the providers/investigators seeking the consent often have no established relationship with the family or patient. The challenges of obtaining consent for patient participation have increased during the COVID-19 pandemic as hospitals have imposed restrictions on visitation by friends or family members who may be able to provide consent on behalf of patients. The COVID-19 pandemic may make patients less willing to seek medical attention or return for follow-up visits post-treatment. In addition, some of our competitors have ongoing clinical trials to treat the same indications as our product candidates, and patients who would otherwise be eligible for our clinical trials may instead enroll in clinical trials of our competitors. If we are not successful at enrolling patients in one clinical trial, it may affect when we are able to initiate the next clinical trial, which could result in significant delays in our efforts to pursue regulatory approval of and commercialize our product candidates. Patient enrollment is affected by other factors including:

- the size and nature of the patient population;
- the severity of the disease under investigation;
- the proximity and availability of clinical trial sites for prospective patients;
- the eligibility criteria for participation in the clinical trial;

- the design of the clinical trial;
- the perceived risks and benefits of the product candidate under study;
- our ability to recruit clinical trial investigators with appropriate experience;
- the availability of drugs approved to treat the diseases under study;
- the patient referral practices of physicians;
- our ability to obtain and maintain patient consents;
- the ability to monitor patients adequately during and after treatment;
- the risk that patients enrolled in clinical trials will drop out of the trials before completion; and
- the impact of public health epidemics, such as the COVID-19 pandemic.

Our inability to enroll a sufficient number of patients for clinical trials would result in significant delays and could require us to abandon one or more clinical trials altogether. Enrollment delays in these clinical trials may result in increased development costs for our product candidates, which would reduce the capital we have available to support current and future product candidates and may result in the need to raise additional capital earlier than planned and could cause the value of our common stock to decline and limit our ability to obtain additional financing.

Our product candidates may cause undesirable side effects or have other properties that could delay or prevent their regulatory approval, limit the commercial potential or result in significant negative consequences following any potential marketing approval.

During the conduct of clinical trials, patients report changes in their health, including illnesses, injuries and discomforts (generally referred to as adverse events), to their doctor. We are required to report adverse events to the FDA and other regulatory authorities. Often, it is not possible to determine whether the product candidate being studied caused these conditions. Regulatory authorities may draw different conclusions or require additional testing to confirm or refute these observations, if they occur. In addition, it is possible that as we test our product candidates in larger, longer and more extensive clinical programs, or as use of these product candidates becomes more widespread if they receive regulatory approval, illnesses, injuries, discomforts and other adverse events that were observed in earlier trials, as well as conditions that did not occur or went undetected in previous trials, will be reported by subjects. Many times, side effects are only detectable after investigational drugs are tested in large-scale, Phase 3 clinical trials or, in some cases, after they are made available to patients on a commercial scale after approval. If additional clinical experience indicates that any of our current product candidates or any future product candidates, have side effects or causes serious or life-threatening side effects, the development of the product candidate may fail or be delayed, or, if the product candidate has received regulatory approval, such approval may be revoked, which could harm our business, prospects, operating results and financial condition.

Moreover, if we elect, or are required, to delay, suspend or terminate any clinical trial of our product candidates, the commercial prospects of our product candidates may be harmed and our ability to generate revenue through their sale may be delayed or eliminated. Any of these occurrences may significantly harm our business, financial condition and prospects.

Additionally, if any of our product candidates receive marketing approval, regulatory authorities may require the addition of labeling statements, such as a “black box” warning or a contraindication, or the adoption of a REMS program to ensure that the benefits outweigh its risks, which may include, among other things, a medication guide outlining the risks of the drug for distribution to patients and a communication plan to health care practitioners, and/or significant restrictions on distribution or use of the drug. Furthermore, if we or others later identify undesirable side effects caused by our product candidates, several potentially significant negative consequences could result, including:

- regulatory authorities may suspend or withdraw approvals of such product candidate;
- regulatory authorities may require additional warnings on the label or impose distribution or use restrictions;
- we may be required to change the way a product candidate is administered or conduct additional clinical trials, including one or more post-market studies;
- we could be sued and held liable for harm caused to patients;

- we may be required to implement a REMS, including the creation of a medication guide outlining the risks of such side effects for distribution to patients, and/or other elements to assure safe use;
- we may need to conduct a recall; and
- our reputation may suffer.

Any of these events could prevent us from achieving or maintaining market acceptance of the affected product candidate, if approved, or could substantially increase commercialization costs and expenses, which could delay or prevent us from generating revenue from the sale of our products and harm our business and results of operations.

Interim "top-line" and preliminary data from our clinical trials that we announce or publish from time to time may change as more patient data become available and are subject to audit and verification procedures that could result in material changes in the final data.

From time to time, we may announce interim top-line or preliminary data from our clinical trials. Interim data from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and/or more patient data become available. Preliminary or top-line data also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, interim and preliminary data should be viewed with caution until the final data are available. Differences between preliminary or interim data and final data could significantly harm our business prospects and may cause the trading price of our common stock to fluctuate significantly.

If we fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs that could harm our business.

We are subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations involve the use of hazardous materials, including chemicals and biological materials. Our operations also produce hazardous waste products. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. We also could incur significant costs associated with civil or criminal fines and penalties for failure to comply with such laws and regulations.

Although we maintain workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with our storage or disposal of biological or hazardous materials.

Risks Related to Our Dependence on Third Parties

We rely on third parties to conduct the clinical trials for our product candidates, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such trials or failing to comply with applicable regulatory requirements.

We have engaged contract research organizations, or CROs, to conduct our ongoing and planned clinical trials. We also expect to engage CROs for any of our other product candidates that may progress to clinical development. We expect to rely on CROs, as well as other third parties, such as clinical data management organizations, medical institutions and clinical investigators, to conduct those clinical trials. Agreements with such third parties might terminate for a variety of reasons, including a failure to perform by the third parties. If we need to enter into alternative arrangements, our product development activities would be delayed.

Our reliance on these third parties for research and development activities will reduce our control over these activities but will not relieve us of our responsibilities. For example, we will remain responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols for the trial. Moreover, the FDA requires us to comply with regulatory standards, commonly referred to as good clinical practices, or GCPs, for conducting, recording and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of trial participants are protected. Similar regulatory requirements apply outside the United States, including the International Council for Harmonisation of Technical Requirements for the Registration of Pharmaceuticals for Human Use, or ICH.

We are also required to register certain ongoing clinical trials and post the results of certain completed clinical trials on government-sponsored, publicly accessible databases, such as ClinicalTrials.gov, within specified timeframes. Failure to do so by us or by third parties can result in FDA refusal to approve applications based on the clinical data, enforcement actions, adverse publicity and civil and criminal sanctions.

Furthermore, these third parties may also have relationships with other entities, some of which may be our competitors. If these third parties do not successfully carry out their contractual duties, meet expected deadlines or conduct our clinical trials in accordance with regulatory requirements or our stated protocols, we will not be able to obtain, or may be delayed in obtaining, marketing approvals for our product candidates and will not be able to, or may be delayed in our efforts to, successfully commercialize our product candidates.

In addition, principal investigators for our clinical trials may serve as scientific advisors or consultants to us from time to time and may receive cash or equity compensation in connection with such services. If these relationships and any related compensation result in perceived or actual conflicts of interest, or the FDA concludes that the financial relationship may have affected the results of the trial, the integrity of the data generated at the applicable clinical trial site may be questioned and the utility of the clinical trial itself may be jeopardized, which could result in the delay or rejection by the FDA of any NDA we submit. Any such delay or rejection could prevent us from commercializing our product candidates.

We also expect to rely on other third parties to store and distribute product supplies for our clinical trials. Any performance failure or regulatory noncompliance on the part of our distributors could delay clinical development or marketing approval of our product candidates or commercialization of our products, resulting in additional losses and depriving us of potential product revenue.

We rely on collaborations with third parties for the development of our product candidates, and we may seek additional collaborations in the future. If those collaborations are not successful, we may not be able to capitalize on the market potential of these product candidates.

We have limited capabilities for drug development, and our product development programs and the commercialization of our product candidates will require substantial additional cash to fund expenses. As a result of these factors, we are, and expect to continue to be, dependent on collaborations relating to the development of our existing and future product candidates. We have had and will continue to have discussions on potential partnering opportunities with various pharmaceutical companies. In addition, we may seek third-party collaborators for the development and commercialization of our product candidates, particularly for the commercialization of our product candidates outside the United States. Likely collaborators for any collaboration arrangements include large and mid-size pharmaceutical companies, regional and national pharmaceutical companies and biotechnology companies and we may face significant competition in seeking appropriate collaborators. If we fail to enter into or maintain collaborations on reasonable terms or at all, our ability to develop our existing or future product candidates could be delayed, the commercial potential of our products could change, and our costs of development and commercialization could increase. If we enter into any future collaboration arrangements with any third parties, we will likely have limited control over the amount and timing of resources that our collaborators dedicate to the development or commercialization of our product candidates. Our ability to generate revenues from these arrangements will depend on our collaborators' abilities to successfully perform the functions assigned to them in these arrangements.

Our collaborations and any future collaborations we might enter into may pose a number of risks, including:

- collaborators often have significant discretion in determining the efforts and resources that they will apply to these collaborations;
- collaborators may not perform their obligations as expected or contractually obligated;
- collaborators may not pursue development and commercialization of any product candidates that achieve regulatory approval or may elect not to continue or renew development or commercialization programs based on clinical trial results, changes in the collaborators' strategic focus or available funding, or external factors, such as an acquisition, that divert resources or create competing priorities;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- product candidates discovered in collaboration with us may be viewed by our collaborators as competitive with their own product candidates or products, which may cause collaborators to cease to devote resources to the commercialization of our product candidates;

- a collaborator with marketing and distribution rights to one or more of our product candidates that achieve regulatory approval may not commit sufficient resources to the marketing and distribution of such products;
- disagreements with collaborators, including disagreements over proprietary rights, contract interpretation or the preferred course of development, might cause delays or termination of the research, development or commercialization of product candidates, might lead to additional responsibilities for us with respect to product candidates, or might result in litigation or arbitration, any of which would be time-consuming and expensive;
- collaborators may not properly maintain or defend our or their intellectual property rights or may use our or their proprietary information in such a way as to invite litigation that could jeopardize or invalidate such intellectual property or proprietary information or expose us to potential litigation;
- collaborators may infringe the intellectual property rights of third parties, which may expose us to litigation and potential liability;
- collaborators may be subject to geo-political actions, natural disasters or other occurrences, including public health epidemics such as the COVID-19 pandemic;
- collaborations may be terminated for the convenience of the collaborator and, if terminated, we could be required to raise additional capital to pursue further development or commercialization of the applicable product candidates; and
- collaborators' decisions may limit the availability of the product supplies required for development, clinical and commercial activities.

Collaboration agreements may not lead to development or commercialization of product candidates in the most efficient manner or at all. If a present or future collaborator were to be involved in a business combination, the continued pursuit and emphasis on our drug development or commercialization program could be delayed, diminished or terminated.

Our reliance on third parties to manufacture our product candidates increases the risk that we will not have sufficient quantities of our product candidates or products or such quantities at an acceptable cost, which could delay, prevent or impair our development or commercialization efforts.

We do not own or operate manufacturing facilities to produce clinical or commercial supplies of the product candidates that we are developing or evaluating. We have limited personnel with experience in drug manufacturing and lack the resources and the capabilities to manufacture any of our product candidates on a clinical or commercial scale. We currently rely on third parties for supply of our product candidates, and our strategy is to outsource all manufacturing of our product candidates and approved products, if any, to third parties.

To conduct clinical trials of our product candidates, we will need to identify suitable manufacturers with the capabilities to manufacture our compounds in large quantities in a manner consistent with existing regulations. Our third-party manufacturers may be unable to successfully increase the manufacturing capacity for any of our product candidates in a timely or cost-effective manner, or at all. In addition, quality issues may arise during scale-up activities and at any other time. If our manufacturers are unable to successfully scale up the manufacture of our product candidates in sufficient quality and quantity, the development, testing and clinical trials of that product candidate may be delayed, or infeasible, and regulatory approval or commercial launch of that product candidate may be delayed or not obtained, which could significantly harm our business.

Even if we can establish and maintain arrangements with third-party manufacturers, reliance on third-party manufacturers entails risks, including:

- reliance on the third party for regulatory compliance and quality assurance;
- the possible breach of the manufacturing agreement by the third party;
- the possible misappropriation of our proprietary information, including our trade secrets and know-how;
- the possible termination or nonrenewal of the agreement by the third party at a time that is costly or inconvenient for us; and
- supply chain disruptions due to geo-political actions, natural disasters or public healthy crises, including epidemics such as the COVID-19 pandemic.

Third-party manufacturers may not be able to comply with cGMP regulations or similar regulatory requirements outside the United States. Our failure, or the failure of our third-party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of product candidates or products, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our product candidates.

Our current and anticipated future dependence upon others for the manufacture of our product candidates may adversely affect our future profit margins and our ability to develop product candidates and commercialize any products that receive marketing approval on a timely and competitive basis.

We may not be able to win government or non-profit contracts or grants to fund our product development activities.

Historically, we have relied in part on funding from contracts or grants from government agencies and non-profit entities and it is part of our strategy to continue to do so. Such contracts or grants can be highly attractive because they provide capital to fund the ongoing development of our product candidates without diluting our stockholders. However, there is often significant competition for these contracts or grants. Entities offering contracts or grants may have requirements to apply for or to otherwise be eligible to receive certain contracts or grants that our competitors may be able to satisfy that we cannot. In addition, such entities may make arbitrary decisions as to whether to offer contracts or make grants, to whom the contracts or grants will be awarded, and the size of the contracts or grants to each awardee. Even if we can satisfy the award requirements, there is no guarantee that we will be selected to receive any contract or grant. If we are not successful in achieving this form of funding for our clinical trials, we will need to seek alternative means of funding which may not be available to the same extent, if at all.

Our reliance on government funding for certain of our programs adds uncertainty to our research, development and commercialization efforts with respect to those programs and may impose requirements that increase the costs of the research, development and commercialization of product candidates developed under those government-funded programs.

Aspects of certain of our development programs are currently being supported, in part, with funding from the NIH, NIAID, CARB-X and the DOD. Contracts and grants awarded by the U.S. government, its agencies and its partners, including our awards from the NIH, NIAID, CARB-X, and the DOD, include provisions that reflect the government's substantial rights and remedies, many of which are not typically found in commercial contracts, including powers of the government to:

- terminate agreements, in whole or in part, for any reason or no reason at all;
- provide grant support to potential competitor programs;
- reduce or modify the government's obligations under such agreements without the consent of the other party;
- claim rights, including intellectual property rights, in products and data developed under such agreements;
- audit contract-related costs and fees, including allocated indirect costs;
- suspend the contractor or grantee from receiving new contracts pending resolution of alleged violations of procurement laws or regulations;
- impose U.S. manufacturing requirements for products that embody inventions conceived or first reduced to practice under such agreements;
- suspend or debar the contractor or grantee from doing future business with the government;
- control and potentially prohibit the export of products;
- pursue criminal or civil remedies under the False Claims Act, False Statements Act and similar remedy provisions specific to government agreements; and
- limit the government's financial liability to amounts appropriated by the U.S. Congress on a fiscal-year basis, thereby leaving some uncertainty about the future availability of funding for a program even after it has been funded for an initial period.

We may not have the right to prohibit the U.S. government from using certain technologies developed by us, and may not be able to prohibit third-party companies, including our competitors, from using those technologies in providing products and services to the

U.S. government. The U.S. government generally takes the position that it has the right to royalty-free use of technologies that are developed under U.S. government contracts.

In addition, government contracts and grants, and subcontracts and subawards awarded in the performance of those contracts and grants, normally contain additional requirements that may increase our costs of doing business, reduce our profits, and expose us to liability for failure to comply with these terms and conditions. These requirements include, for example:

- specialized accounting systems unique to government awards;
- mandatory financial audits and potential liability for price adjustments or recoupment of government funds after such funds have been spent;
- adhering to stewardship principles imposed by CARB-X as a condition of the award;
- public disclosures of certain award information, which may enable competitors to gain insights into our research program; and
- mandatory socioeconomic compliance requirements, including labor standards, non-discrimination and affirmative action programs and environmental compliance requirements.

As an organization, we are relatively new to government contracting and new to the regulatory compliance obligations that such contracting entails. If we fail to maintain compliance with those obligations, we may be subject to potential liability and termination of our contracts.

As a U.S. government contractor, we are subject to financial audits and other reviews by the U.S. government of our costs and performance on our contracts, as well as our accounting and general business practices related to these contracts. Based on the results of its audits, the government may adjust our contract-related costs and fees, including allocated indirect costs.

Risks Related to the Commercialization of Our Product Candidates

Even if any of our product candidates receives marketing approval, such product candidate may fail to achieve the degree of market acceptance by physicians, patients, third-party payors and others in the medical community necessary for commercial success.

Even if we obtain approvals from the FDA, the EMA or other comparable regulatory agencies and can initiate commercialization of a product candidate we develop, the product candidate may not achieve market acceptance among physicians, patients, hospitals, including pharmacy directors, and third-party payors and, ultimately, may not be commercially successful. The degree of market acceptance of our product candidates, if approved for commercial sale, will depend on several factors, including:

- the efficacy and potential advantages compared to alternative treatments;
- the potential and perceived advantages and disadvantages of the product candidates, including cost and clinical benefit relative to alternative treatments;
- the convenience and ease of administration compared to alternative treatments;
- the willingness of the target patient population to try new therapies and of physicians to prescribe these therapies;
- acceptance by physicians, patients, operators of hospitals, including in-hospital formularies, and treatment facilities and parties responsible for coverage and reimbursement of the product;
- the availability of coverage and adequate reimbursement by third-party payors and government authorities;
- the ability to manufacture our product in sufficient quantities and yields;
- the strength and effectiveness of marketing and distribution support;
- the prevalence and severity of any side effects;

- limitations or warnings, including distribution or use restrictions, contained in the product's approved labeling or an approved REMS;
- whether the product is designated under physician treatment guidelines as a first-line therapy or as a second- or third-line therapy for particular infections;
- the approval of other new products for the same indications;
- the timing of market introduction of the approved product as well as competitive products;
- the emergence of bacterial resistance to the product; and
- the rate at which resistance to other drugs in the target infections grow.

Any failure by any of our product candidates that obtains regulatory approval to achieve market acceptance or commercial success could have a material adverse effect on our business prospects.

We face substantial competition, which may result in others discovering, developing, or commercializing products before or more successfully than we do.

The development and commercialization of new drug products is highly competitive. We face competition from major multi-national pharmaceutical companies, biotechnology companies, specialty pharmaceutical companies and generic drug companies with respect to our current and future product candidates. There are several large pharmaceutical and biotechnology companies that currently market and sell products or are pursuing the development of product candidates for the treatment of drug-resistant infections. Potential competitors also include academic institutions, government agencies and other public and private research organizations. Our competitors may succeed in developing, acquiring or licensing technologies and drug products that are more effective, more effectively marketed and sold or less costly than our product candidates, which could render our product candidates non-competitive and obsolete.

If our competitors obtain marketing approval from the FDA, the EMA or other comparable regulatory authorities for their product candidates more rapidly than we do, it could result in our competitors establishing a strong market position before we are able to enter the market.

Many of such our competitors have greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products than we do as an organization. Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller and other early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These third parties compete with us in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than any product candidates that we may develop. Our competitors also may obtain approval from the FDA, the EMA or other comparable regulatory agencies for their product candidates more rapidly than we may obtain approval for ours, which could result in product approval delays if a competitor obtains market exclusivity from the FDA or the EMA, or our competitors establish a strong market position before we are able to enter the market. In addition, our ability to compete may be affected in many cases by insurers or other third-party payors seeking to encourage the use of generic drugs. Additional drugs may become available on a generic basis over the coming years. If our product candidates achieve marketing approval, we expect that they will be priced at a significant premium over competitive generic drugs.

Coverage and adequate reimbursement may not be available for our current or any future product candidates, which could make it difficult for us to sell profitably, if approved.

Market acceptance and sales of any product candidates that we or our collaborators commercialize will depend in part on the extent to which reimbursement for these drugs and related treatments will be available from third-party payors, including government health care programs (such as Medicare and Medicaid), government health administration authorities, managed care organizations and other private health insurers. Third-party payors decide which therapies they will pay for and establish reimbursement levels. Third-party payors often rely upon Medicare coverage policy and payment limitations in setting their own coverage and reimbursement policies. However, decisions regarding the extent of coverage and amount of reimbursement to be provided for any product candidates that we develop will be made on a payor-by-payor basis. One payor's determination to provide coverage for a drug does not assure

that other payors will also provide coverage and adequate reimbursement for the drug. Additionally, a third-party payor's decision to provide coverage for a therapy does not imply that an adequate reimbursement rate will be approved. Each payor determines whether it will provide coverage for a therapy, what amount it will pay the manufacturer for the therapy, and on what tier of its list of covered drugs, or formulary, it will be placed. The position on a payor's formulary generally determines the co-payment that a patient will need to make to obtain the therapy and can strongly influence the adoption of such therapy by patients and physicians. Patients who are prescribed treatments for their conditions and providers prescribing such services generally rely on third-party payors to reimburse all or part of the associated healthcare costs. Patients are unlikely to use our drugs, and providers are unlikely to prescribe our drugs, unless coverage is provided, and reimbursement is adequate to cover a significant portion of the cost of our drugs and their administration.

A primary trend in the United States healthcare industry and elsewhere is cost containment. Third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. We cannot be sure that coverage and reimbursement will be available for any drug that we commercialize and, if reimbursement is available, what the level of reimbursement will be. Inadequate coverage and reimbursement may impact the demand, or the price of, any drug for which we obtain marketing approval for. If coverage and adequate reimbursement are not available, or are available only to limited levels, we may not be able to successfully commercialize our current and any future product candidates that we develop.

Product liability lawsuits against us could cause us to incur substantial liabilities and to limit commercialization of any products that we may develop.

We face an inherent risk of product liability exposure related to the testing of our product candidates in human clinical trials and will face an even greater risk if we commercially sell any drugs that we may develop. If we cannot successfully defend ourselves against claims that our product candidates or products caused injuries, we will incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- reduced resources of our management to pursue our business strategy;
- decreased demand for any product candidates or products that we may develop;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial participants;
- initiation of investigations by regulators;
- product recalls, withdrawals or labeling, marketing or promotional restrictions;
- significant costs to defend the resulting litigation;
- substantial monetary awards paid to clinical trial participants or patients;
- loss of revenue; and
- the inability to commercialize any drugs that we may develop.

We currently hold product liability insurance coverage in an amount that may not be adequate to cover all liabilities that we may incur. We may need to increase our insurance coverage as we expand our clinical trials or if we commence commercialization of our product candidates. Insurance coverage is increasingly expensive. We may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise.

There are a variety of risks associated with marketing our product candidates internationally, which could affect our business.

We or our collaborators may seek regulatory approval for our product candidates outside of the United States and, accordingly, we expect that we will be subject to additional risks related to operating in foreign countries if we obtain the necessary approvals, including:

- differing regulatory requirements in foreign countries;
- the potential for so-called parallel importing, which is what happens when a local seller, faced with high or higher local prices, opts to import goods from a foreign market with low or lower prices rather than buying them locally;

- unexpected changes in tariffs, trade barriers, price and exchange controls and other regulatory requirements;
- economic weakness, including inflation, or political instability in foreign economies and markets;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- foreign taxes, including withholding of payroll taxes;
- foreign currency fluctuations, which could result in increased operating expenses and reduced revenues, and other obligations incident to doing business in another country;
- difficulties staffing and managing foreign operations;
- workforce uncertainty in countries where labor unrest is more common than in the United States;
- reduced level of reimbursement, pricing and insurance regimes compared to the United States;
- potential liability under the Foreign Corrupt Practices Act of 1977 or comparable foreign regulations;
- challenges enforcing our contractual and intellectual property rights, especially in those foreign countries that do not respect and protect intellectual property rights to the same extent as the United States;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad; and
- business interruptions resulting from geo-political actions, including war and terrorism, or natural disasters including earthquakes, typhoons, floods, fires, and public health epidemics, such as the COVID-19 pandemic.

These and other risks associated with our international operations may compromise our ability to achieve or maintain profitability.

Risks Related to Our Business and Managing Our Growth

We have pursued and may continue to pursue acquisitions. Acquisitions could be difficult to integrate, divert the attention of key personnel, disrupt our business, dilute stockholder value and impair our financial results.

As part of our business strategy, we have pursued and intend to continue to pursue acquisitions of complementary businesses, products, services or technologies that we believe could accelerate our ability to compete in our existing markets or allow us to enter new markets. Any of these transactions could be material to our financial condition and results of operations. If we fail to properly evaluate or integrate acquisitions, we may not achieve the anticipated benefits of any such acquisitions, and we may incur costs in excess of what we anticipate. The failure to successfully evaluate and execute acquisitions or otherwise adequately address these risks could materially harm our business and financial results.

Acquisitions also frequently result in the recording of goodwill and other intangible assets which are subject to potential impairments which could harm our financial results. As a result, if we fail to properly evaluate acquisitions or investments, we may not achieve the anticipated benefits of any such acquisitions, and we may incur costs in excess of what we anticipate. The failure to successfully evaluate and execute acquisitions or investments or otherwise adequately address these risks could materially harm our business and financial results.

We might not be able to successfully integrate our operations with those of Entasis and/or La Jolla and other assets that we may acquire.

We completed the acquisition of Entasis on July 11, 2022, pursuant to which Entasis became a wholly owned subsidiary of Innoviva and the acquisition of La Jolla, on August 22, 2022, pursuant to which La Jolla became a wholly owned subsidiary of Innoviva. Our integration of the operations and personnel of each of Entasis and La Jolla and any other assets we may acquire may require significant efforts, including significant amounts of management's time, and result in additional expenses. Factors that will affect the success of the acquisitions include the strength of our combined product pipelines, our ability to execute our business strategy, our ability to adequately fund research and development and retain key employees, and results of clinical trials, regulatory approvals and reimbursement levels of any approved product. In addition, we cannot be certain that any technology or assets we acquire will be successfully developed, become profitable or remain so.

Failure to realize the anticipated benefits from our acquisition of Entasis and La Jolla may affect our future results of operations and financial operations.

In connection with our acquisition of Entasis and La Jolla, we have integrated the research and development, commercial operations and personnel into our existing infrastructure. If there are unexpected difficulties in our integration of these acquired businesses, the anticipated benefits of the transaction may not be realized or may take longer to realize than expected. The anticipated benefits of the acquisition could be materially reduced by a number of factors, including the following:

- the future revenue and gross margins of the acquired products may be materially different from those we originally anticipated;
- we could incur material unanticipated expenses;
- claims or lawsuits may arise from the acquisition transaction or from their previous business operations;
- we may experience difficulties in implementing effective internal controls over financial reporting as part of our integration actions; and
- potential growth, expected financial results, perceived synergies and anticipated opportunities may not be realized through the ongoing integration actions.

The occurrence of any or all of these events may have an adverse effect on our business and results of operations.

If we engage in future acquisitions or strategic collaborations, this may increase our capital requirements, dilute our stockholders, cause us to incur debt or assume contingent liabilities and subject us to other risks.

From time to time, we may evaluate various acquisitions and strategic collaborations, including licensing or acquiring complementary drugs, intellectual property rights, technologies or businesses, as deemed appropriate to carry out our business plan. Any potential acquisition or strategic collaboration may entail numerous risks, including:

- increased operating expenses and cash requirements;
- the assumption of additional indebtedness or contingent liabilities;
- assimilation of operations, intellectual property and drugs of an acquired company, including challenges associated with integrating new personnel;
- the diversion of our management's attention from our existing drug programs and initiatives in pursuing such a strategic partnership, merger or acquisition;
- retention of key employees, the loss of key personnel and uncertainties in our ability to maintain key business relationships;
- risks and uncertainties associated with the other party to such a transaction, including the prospects of that party and their existing drugs or drug candidates and regulatory approvals; and
- our inability to generate revenue from acquired technology and/or drugs sufficient to meet our objectives in undertaking the acquisition or even to offset the associated acquisition and maintenance costs.

Risks Related to Our Intellectual Property

If we are unable to obtain and maintain patent protection for our technology and product candidates, or if the scope of the patent protection obtained is not sufficiently broad, our competitors could develop and commercialize technology and drugs similar or identical to ours, and our ability to successfully commercialize our technology and product candidates may be adversely affected.

Our success depends in large part on our ability to obtain and maintain patent protection in the United States and other countries with respect to our product candidates. We seek to protect our proprietary position by filing patent applications in the United States and abroad related to our technology and product candidates. If we do not adequately protect our intellectual property, competitors may be able to use our technologies and erode or negate any competitive advantage that we may have, which could harm our business

and ability to achieve profitability. To protect our proprietary positions, we file patent applications in the United States and abroad related to our novel technologies and product candidates that are important to our business.

The patent application and prosecution process are expensive and time-consuming. We, our current licensees, or any future licensors and licensees may not be able to file and prosecute all necessary or desirable patent applications at a reasonable cost or in a timely manner. We or our current licensees, or any future licensors or licensees may also fail to identify patentable aspects of our research and development before it is too late to obtain patent protection.

Therefore, these and any of our patents and applications may not be prosecuted and enforced in a manner consistent with our best interests. It is possible that defects of form in the preparation or filing of our patents or patent applications may exist, or may arise in the future, such as with respect to proper priority claims, inventorship, claim scope or patent term adjustments. If our current licensees, or any future licensors or licensees, are not fully cooperative or disagree with us as to the prosecution, maintenance or enforcement of any patent rights, such patent rights could be compromised, and we might not be able to prevent third parties from making, using and selling competing products. If there are material defects in the form or preparation of our patents or patent applications, such patents or applications may be invalid and/or unenforceable. Moreover, our competitors may independently develop equivalent knowledge, methods and know-how. Any of these outcomes could impair our ability to prevent competition from third parties.

The patent position of biotechnology and pharmaceutical companies generally is highly uncertain. Changes in either the patent laws or interpretation of the patent laws in the United States and other countries may diminish the value of our patents or narrow the scope of our patent protection. In addition, the laws of foreign countries may not protect our rights to the same extent as the laws of the United States. No consistent policy regarding the breadth of claims allowed in biotechnology and pharmaceutical patents has emerged to date in the United States or in many foreign jurisdictions. For example, European patent law currently restricts the patentability of methods of treatment of the human body more than United States law does. In addition, the determination of patent rights with respect to pharmaceutical compounds and technologies commonly involves complex legal and factual questions, which has in recent years been the subject of much litigation. As a result, the issuance, scope, validity, enforceability and commercial value of our patent rights are highly uncertain. Furthermore, recent changes in patent laws in the United States, including the America Invents Act of 2011, may affect the scope, strength and enforceability of our patent rights or the nature of proceedings that may be brought by us related to our patent rights.

We may not be aware of all third-party intellectual property rights potentially relating to our current and future product candidates. Publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing, or in some cases not at all. Therefore, we cannot be certain that we were the first to make the inventions claimed in our patents or pending patent applications, or that we were the first to file for patent protection of such inventions. Similarly, should we own any patents or patent applications in the future, we may not be certain that we were the first to file for patent protection for the inventions claimed in such patents or patent applications. As a result, the issuance, scope, validity and commercial value of our patent rights cannot be predicted with any certainty. Moreover, we may be subject to a third-party pre-issuance submission of prior art to the U.S. Patent and Trademark Office, or USPTO, or become involved in derivation, ex-parte reexamination, or inter partes review proceedings in the USPTO or similar proceedings elsewhere, challenging our patent rights or the patent rights of others. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate, our patent rights, allow third parties to commercialize our technology or product candidates and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize products without infringing third-party patent rights. If the breadth or strength of protection provided by our patents and patent applications is threatened, regardless of the outcome, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates.

Our pending and future patent applications may not result in patents being issued that protect our technology or product candidates, in whole or in part, or which effectively prevent others from commercializing competitive technologies and products. Even if our patent applications issue as patents, they may not issue in a form that will provide us with any meaningful protection against competing products or processes sufficient to achieve our business objectives, prevent competitors from competing with us or otherwise provide us with any competitive advantage. Our competitors may be able to circumvent our owned or licensed patents by developing similar or alternative technologies or products in a non-infringing manner. Our competitors may seek to market generic versions of any approved products by submitting abbreviated new drug applications to the FDA in which they claim that patents owned or licensed by us are invalid, unenforceable and/or not infringed. Alternatively, our competitors may seek approval to market their own products similar to or otherwise competitive with our products. In these circumstances, we may need to defend and/or assert our patents, including by filing lawsuits alleging patent infringement. In any of these types of proceedings, a court or other agency with jurisdiction may find our patents invalid and/or unenforceable.

The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our owned and licensed patents may be challenged in the courts or patent offices in the United States and abroad. Such challenges may result in loss of

exclusivity or freedom to operate, a patent being held unenforceable, and/or in one or more or in patent claims being narrowed or invalidated or held unenforceable, in whole or in part, which could limit our ability to stop others from using or commercializing similar or identical technology and products or limit the duration of the patent protection of our technology and products.

Patent terms may be inadequate to protect our competitive position on our product candidates for an adequate amount of time.

Patents have a limited lifespan. In the U.S., if all maintenance fees are timely paid, the natural expiration of a patent is generally 20 years from its earliest filing date of a non-provisional application to which the patent claims priority. Various extensions may be available, but the life of a patent, and the protection it affords, is limited. Even if patents covering our product candidates are obtained, once the patent life has expired for a product candidate, we may be open to competition from competitive medications, including generic medications. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such product candidates might expire before or shortly after such product candidates are commercialized. As a result, our owned and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing product candidates similar or identical to ours.

In addition, given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting our candidates might expire before or shortly after our candidates are commercialized. Depending upon the timing, duration and conditions of any FDA marketing approval of our product candidates, one or more of our U.S. patents may be eligible for limited patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984, referred to as the Hatch-Waxman Amendments, and similar legislation in the European Union, as discussed above. As a result, our revenue from applicable products could be reduced. Further, if this occurs, our competitors may take advantage of our investment in development and trials by referencing our clinical and preclinical data and launch their product earlier than might otherwise be the case, and our competitive position, business, financial condition, results of operations, and prospects could be materially harmed.

We may need to license intellectual property from third parties, and such licenses may not be available or may not be available on commercially reasonable terms.

A third party may hold intellectual property rights, including patent rights, that are important or necessary to the development of our product candidates. It may be necessary for us to use the patented or proprietary technology of third parties to commercialize our product candidates, in which case we would be required to obtain a license from these third parties. Such a license may not be available on commercially reasonable terms, or at all, and we could be forced to accept unfavorable contractual terms. If we are unable to obtain such licenses on commercially reasonable terms, our business could be harmed.

If we are unable to obtain rights to required third-party intellectual property rights or maintain the existing intellectual property rights we have, we may be required to expend significant time and resources to redesign our technology, product candidates, or the methods for manufacturing them or to develop or license replacement technology, all of which may not be feasible on a technical or commercial basis. If we are unable to do so, we may be unable to develop or commercialize the affected technology and product candidates, which could materially harm our business, financial condition, results of operations, and prospects.

We may become involved in lawsuits to protect or enforce our patents or other intellectual property, which could be expensive, time-consuming and unsuccessful.

Competitors and other third parties may infringe our issued patents, trademarks, copyrights or other intellectual property. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time-consuming and divert the time and attention of our management and scientific personnel. Any claims we assert against perceived infringers could provoke these parties to assert counterclaims against us alleging that we infringe their patents, trademarks, copyrights or other intellectual property. In addition, in a patent infringement proceeding, there is a risk that a court will decide that a patent of ours is invalid or unenforceable or that one or more claims of a patent are invalid, in whole or in part, and that we do not have the right to stop the other party from using the invention at issue. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO, or made a misleading statement, during prosecution. There is also a risk that, even if the validity of such patents is upheld, the court will construe the patent's claims narrowly or decide that we do not have the right to stop the other party from using the invention at issue on the basis that our patents do not cover the invention. An adverse outcome in a litigation or proceeding involving our patents could limit our ability to assert our patents against those parties or other competitors and may curtail or preclude our ability to exclude third parties from making and selling similar or competitive products. Similarly, if we assert trademark infringement claims, a court may determine that the marks we have asserted are invalid or unenforceable, or that the party against whom we have asserted trademark infringement has superior rights to the marks in question. In this case, we could ultimately be forced to cease use of such trademarks.

In any infringement litigation, any award of monetary damages we receive may not be commercially valuable. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during litigation. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. Moreover, there can be no assurance that we will have sufficient financial or other resources to file and pursue such infringement claims, which typically last for years before they are concluded. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources and more mature and developed intellectual property portfolios. Even if we ultimately prevail in such claims, the monetary cost of such litigation and the diversion of the attention of our management and scientific personnel could outweigh any benefit we receive because of the proceedings. Accordingly, despite our efforts, we may not be able to prevent third parties from infringing, misappropriating or successfully challenging our intellectual property rights. Uncertainties resulting from the initiation and continuation of patent litigation or other proceedings could have a negative impact on our ability to compete in the marketplace.

Third parties may initiate legal proceedings alleging that we are infringing their intellectual property rights, the outcome of which would be uncertain and could significantly harm our business.

There is a substantial amount of intellectual property litigation in the biotechnology and pharmaceutical industries, and we may become party to, or threatened with, litigation or other adversarial proceedings regarding intellectual property rights with respect to our technology or product candidates, including interference proceedings before the USPTO. Intellectual property disputes arise in several areas including with respect to patents, use of other proprietary rights and the contractual terms of license arrangements. Third parties may assert claims against us based on existing or future intellectual property rights. The outcome of intellectual property litigation is subject to uncertainties that cannot be adequately quantified in advance.

If we are found to infringe a third-party's intellectual property rights, we could be forced, including by court order, to cease developing, manufacturing or commercializing the infringing product candidate or product. Alternatively, we may be required to obtain a license from such third party to use the infringing technology and continue developing, manufacturing or marketing the infringing product candidate. However, we may not be able to obtain any required license on commercially reasonable terms or at all. Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors access to the same technologies licensed to us. In addition, we could be found liable for monetary damages, including treble damages and attorneys' fees if we are found to have willfully infringed a patent. A finding of infringement could prevent us from commercializing our product candidates or force us to cease some of our business operations. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar negative effect on our business.

We may not be able to protect our intellectual property rights throughout the world.

Filing, prosecuting and defending patents on product candidates in all countries throughout the world would be prohibitively expensive, and our intellectual property rights in some countries outside the United States could be less extensive than those in the United States. In some cases, we may not be able to obtain patent protection for certain licensed technology outside the United States. In addition, the laws of some foreign countries do not protect intellectual property rights to the same extent as federal and state laws in the United States, even in jurisdictions where we do pursue patent protection. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, even in jurisdictions where we do pursue patent protection or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions.

Competitors may use our technologies in jurisdictions where we have not pursued and obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we have patent protection, but enforcement is not as strong as that in the United States. These products may compete with our product candidates and preclinical programs and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in foreign jurisdictions. The legal systems of certain countries, particularly certain developing countries, do not favor the enforcement of patents, trade secrets and other intellectual property protection, particularly those relating to biotechnology products, which could make it difficult for us to stop the infringement of our patents, if pursued and obtained, or marketing of competing products in violation of our proprietary rights generally. Proceedings to enforce our patent rights in foreign jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly and our patent applications at risk of not issuing and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate, and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our

efforts to enforce our intellectual property rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

If we are unable to protect the confidentiality of our trade secrets, our business and competitive position would be harmed.

In addition to seeking patent and trademark protection for our product candidates, we also rely on trade secrets, including unpatented know-how, technology and other proprietary information, to maintain our competitive position. We seek to protect our trade secrets, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to them, such as our employees, corporate collaborators, outside scientific collaborators, contract manufacturers, consultants, advisors and other third parties prior to beginning research or disclosing proprietary information. We also enter into confidentiality and invention or patent assignment agreements with our employees and consultants. Despite these efforts, any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets. Despite these efforts and the contractual provisions employed when working with third parties, the need to share trade secrets and other confidential information due to our reliance on third parties, increases the risk that such trade secrets become known by our competitors, are inadvertently incorporated into the technology of others, or are disclosed or used in violation of these agreements.

Monitoring unauthorized uses and disclosures of our intellectual property is difficult, and we do not know whether the steps we have taken to protect our intellectual property will be effective. In addition, we may not be able to obtain adequate remedies for any such breaches. Enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. In addition, some courts inside and outside the United States are less willing or unwilling to protect trade secrets.

Moreover, our competitors may independently develop knowledge, methods and know-how equivalent to our trade secrets. Competitors could purchase our products and replicate some or all the competitive advantages we derive from our development efforts for technologies on which we do not have patent protection. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor, we would have no right to prevent them, or those to whom they communicate it, from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor, our competitive position would be harmed.

Risks Related to Regulatory Approval of Our Product Candidates and Other Legal Compliance Matters

Even if we complete the necessary preclinical studies and clinical trials, the regulatory approval process is expensive, time-consuming and uncertain and may prevent us or any future collaborators from obtaining approvals for the commercialization of some or all of our product candidates. As a result, we cannot predict when or if, and in which territories, we, or any future collaborators, will obtain marketing approval to commercialize a product candidate.

Our product candidates and the activities associated with their development and commercialization, including their design, research, testing, manufacture, safety, efficacy, quality control, recordkeeping, labeling, packaging, storage, approval, advertising, promotion, sale, distribution, import, export, and reporting of safety and other post-market information, are subject to comprehensive regulation by the FDA, the EMA and other foreign regulatory agencies. Failure to obtain marketing approval for a product candidate will prevent us or a potential collaborator from commercializing the product candidate. We will rely on third parties to assist us in the process of filing and supporting the applications necessary to gain marketing approvals. Securing marketing approval requires the submission of extensive preclinical and clinical data and supporting information to regulatory authorities for each therapeutic indication to establish the product candidate's safety and efficacy. Securing marketing approval also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities by, the regulatory authorities. Our product candidates may not be effective, may be only moderately effective or may prove to have undesirable or unintended side effects, toxicities or other characteristics that may preclude our obtaining marketing approval or prevent or limit commercial use. We may not be able to successfully manufacture our products in compliance with applicable requirements such as GMPs. If any of our product candidates receives marketing approval, the accompanying label may limit its approved use more narrowly than we anticipate, which could limit sales of the product.

The process of obtaining marketing approvals, both in the United States and abroad, is expensive and may take many years, if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity and novelty of the product candidates involved. Securing marketing approval requires the submission of extensive preclinical and clinical data and supporting information to regulatory authorities for each therapeutic indication to establish the product candidate's safety and efficacy. Securing marketing approval also requires the submission of information about the product manufacturing process to, and inspection of manufacturing facilities by, the regulatory authorities. The FDA, the EMA or other regulatory authorities may determine that our product candidates are not safe and effective, only moderately effective or have undesirable or unintended side effects, toxicities or other characteristics that preclude us from obtaining marketing approval or prevent or limit commercial use. Any marketing approval

we ultimately obtain may be limited or subject to restrictions or post-approval commitments that render the approved product not commercially viable.

In addition, changes in marketing approval policies during the development period, changes in or the enactment of additional statutes or regulations, or changes in regulatory review for each submitted product application, may cause delays in the approval or rejection of an application. Regulatory authorities have substantial discretion in the approval process and may refuse to accept any application or may decide that our data is insufficient for approval and require additional preclinical, clinical or other studies. In addition, varying interpretations of the data obtained from preclinical and clinical testing could delay, limit or prevent marketing approval of a product candidate. Any marketing approval we ultimately obtain may be limited or subject to restrictions or post-approval commitments that render the approved product not commercially viable. Any marketing approval that we, or any future collaborators, ultimately obtain may be limited or subject to restrictions or post-approval commitments that render the approved product not commercially viable.

If we experience delays in obtaining approval or if we fail to obtain approval of our product candidates, the commercial prospects for our product candidates may be harmed and our ability to generate revenues will be impaired.

Failure to obtain marketing approval in foreign jurisdictions would prevent certain of our product candidates from being marketed in these territories. Any approval we are granted for our product candidates in the United States would not assure approval of our product candidates in foreign jurisdictions.

To market and sell our products in the European Union, or EU, and any other jurisdictions, we must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. The approval procedure varies among countries and can involve additional testing. The time required to obtain approval may differ substantially from that required to obtain approval from the FDA. The regulatory approval process outside the United States generally includes all the risks associated with obtaining approval from the FDA. In addition, in many countries outside the United States, it is required that the product be approved for reimbursement before the product can be approved for sale in that country. We may not obtain approvals from regulatory authorities outside the United States on a timely basis, if at all. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one regulatory authority outside the United States does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA. However, denial of approval in one jurisdiction may impact the ability to obtain approval elsewhere. We may not be able to file for marketing approvals and may not receive necessary approvals to commercialize our products in any market.

Even if we obtain marketing approvals for our product candidates, the terms of approvals and ongoing regulation of our products may limit how we or our collaborators manufacture and market our products and compliance with such requirements may involve substantial resources, which could materially impair our ability to generate revenue.

Even if marketing approval of a product candidate is granted, an approved product and its manufacturer and marketer are subject to ongoing review and extensive regulation, including the potential requirements to implement a REMS or to conduct costly post-marketing studies or clinical trials and surveillance to monitor the safety or efficacy of the product. We must also comply with requirements concerning advertising and promotion for any of our product candidates for which we obtain marketing approval. Promotional communications with respect to prescription drugs are subject to a variety of legal and regulatory restrictions and must be consistent with the information in the product's approved labeling. Thus, we will not be able to promote any products we develop for indications or uses for which they are not approved. In addition, manufacturers of approved products and those manufacturers' facilities are required to comply with extensive FDA requirements including ensuring that quality control and manufacturing procedures conform to cGMP, which include requirements relating to quality control and quality assurance as well as the corresponding maintenance of records and documentation and reporting requirements, among other things. We and our contract manufacturers could be subject to periodic unannounced inspections by the FDA to monitor and ensure compliance with cGMP. We must also comply with FDA requirements for adverse event reporting for commercial products.

Accordingly, assuming we receive marketing approval for one or more of our product candidates, we and our contract manufacturers will continue to expend time, money and effort in all areas of regulatory compliance, including manufacturing, production, product surveillance and quality control. If we are not able to comply with post-approval regulatory requirements, we could have the marketing approvals for our products withdrawn by regulatory authorities and our ability to market any future products could be limited, which could adversely affect our ability to achieve or sustain profitability. We could also be subject to other civil or criminal penalties. Thus, the cost of compliance with post-approval regulations may have a negative effect on our operating results and financial condition.

Any product candidate for which we obtain marketing approval could be subject to post-marketing restrictions or recall or withdrawal from the market, and we may be subject to penalties if we fail to comply with regulatory requirements or if we experience unanticipated problems with our product candidates, when and if any of them are approved.

The FDA and other federal and state agencies, including the U.S. DOJ, closely regulate compliance with all requirements governing prescription drug products, including requirements pertaining to marketing and promotion of drugs in accordance with the provisions of the approved labeling and manufacturing of products in accordance with cGMP requirements. The FDA and DOJ impose stringent restrictions on manufacturers' communications regarding off-label use and if we market our products for indications other than their approved indications, we may be subject to enforcement action for off-label marketing. Violations of such requirements may lead to investigations alleging violations of the Food, Drug and Cosmetic Act and other statutes, including the False Claims Act and other federal and state health care fraud and abuse laws as well as state consumer protection laws.

Our failure to comply with all regulatory requirements, and later discovery of previously unknown adverse events or other problems with our products, manufacturers or manufacturing processes, may yield various results, including:

- litigation involving patients taking our products;
- restrictions on our products, manufacturers or manufacturing processes;
- restrictions on the labeling or marketing of a product;
- restrictions on product distribution or use;
- requirements to conduct post-marketing studies or clinical trials;
- warning or untitled letters;
- withdrawal of the products from the market;
- refusal to approve pending applications or supplements to approve applications that we submit;
- recall of products;
- fines, restitution or disgorgement of profits or revenues;
- suspension or withdrawal of marketing approvals;
- damage to relationships with any potential collaborators;
- unfavorable press coverage and damage to our reputation;
- refusal to permit the import or export of our products;
- product seizure; or
- injunctions or imposition of civil or criminal penalties.

Non-compliance by us or any future collaborator with regulatory requirements regarding safety monitoring or pharmacovigilance, and with requirements related to the development of products for the pediatric population, can also result in significant financial penalties. Similarly, failure to comply with regulatory requirements regarding the protection of personal information can also lead to significant penalties and sanctions.

Non-compliance with U.K. and EU requirements regarding safety monitoring or pharmacovigilance, and with requirements related to the development of products for the pediatric population, also can result in significant financial penalties. Similarly, failure to comply with the U.K.'s or EU's requirements regarding the protection of personal information can also lead to significant penalties and sanctions.

Our current and future relationships with healthcare professionals, principal investigators, consultants, customers and third-party payors in the United States and elsewhere may be subject, directly or indirectly, to applicable anti-kickback, fraud and abuse, false claims, physician payment transparency, health information privacy and security and other healthcare laws and regulations, which could expose us to penalties.

Our current and future arrangements with healthcare professionals, principal investigators, consultants, customers and third-party payors may expose us to broadly applicable fraud and abuse and other healthcare laws, including, without limitation, the federal Anti-Kickback Statute and the federal False Claims Act, that may constrain the business or financial arrangements and relationships through which we research, sell, market and distribute any product candidates for which we obtain marketing approval. In addition, we may be subject to physician payment transparency laws and patient privacy and security regulation by the federal government and by the states and foreign jurisdictions in which we conduct our business. The applicable federal, state and foreign healthcare laws that may affect our ability to operate include the following:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, lease, order or recommendation of, any good, facility, item or service, for which payment may be made, in whole or in part, under federal healthcare programs such as Medicare and Medicaid;

- federal civil and criminal false claims laws, including the federal False Claims Act, which impose criminal and civil penalties, including through civil whistleblower or *qui tam* actions, against individuals or entities for, among other things, knowingly presenting, or causing to be presented, to the federal government, including the Medicare and Medicaid programs, claims for payment that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government;

- the civil monetary penalties statute, which imposes penalties against any person or entity who, among other things, is determined to have presented or caused to be presented a claim to a federal health program that the person knows or should know is for an item or service that was not provided as claimed or is false or fraudulent;

- HIPAA, which created additional federal criminal and civil statutes that prohibit knowingly and willfully executing, or attempting to execute, a scheme to defraud any healthcare benefit program or obtain, by means of false or fraudulent pretenses, representations or promises, any of the money or property owned by, or under the custody or control of, any healthcare benefit program, regardless of whether the payor is public or private, knowingly and willfully embezzling or stealing from a health care benefit program, willfully obstructing a criminal investigation of a health care offense and knowingly and willfully falsifying, concealing or covering up by any trick or device a material fact or making any materially false statements in connection with the delivery of, or payment for, healthcare benefits, items or services relating to healthcare matters;

- HIPAA, as amended by the HITECH Act of 2009, and their respective implementing regulations, which impose obligations on "covered entities," including certain healthcare providers, health plans, and healthcare clearinghouses, as well as their respective "business associates" that create, receive, maintain or transmit individually identifiable health information for or on behalf of a covered entity, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;

- the federal Physician Payments Sunshine Act, created under Section 6002 of Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or collectively, the ACA, and its implementing regulations, which created annual reporting requirements for manufacturers of drugs, devices, biologicals and medical supplies for certain payments and "transfers of value" provided to covered recipients, including physicians, as defined by such law, and teaching hospitals, as well as ownership and investment interests held by physicians and their immediate family members; and

- analogous state and foreign laws, such as state anti-kickback and false claims laws, which may apply to sales or marketing arrangements and claims involving healthcare items or services reimbursed by non-governmental third-party payors, including private insurers; state and foreign laws that require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government or to adopt compliance programs as prescribed by state laws and regulations, or that otherwise restrict payments that may be made to healthcare providers; state and foreign laws that require drug manufacturers to report information related to payments and other transfers of value to physicians and other healthcare providers or marketing expenditures and drug pricing; state and local laws requiring the licensure of pharmaceutical sales representatives; and state and foreign laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Further, the ACA, among other things, amended the intent requirement of the federal Anti-Kickback Statute and certain criminal statutes governing healthcare fraud. A person or entity no longer needs to have actual knowledge of the statute or specific intent to violate it. In addition, the ACA provided that the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the False Claims Act.

Efforts to ensure that our future business arrangements with third parties will comply with applicable healthcare laws and regulations may involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, including, without limitation, damages, monetary fines, disgorgement, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, contractual damages, reputational harm, diminished profits and future earnings, additional reporting or oversight obligations if we become subject to a corporate integrity agreement or other agreement to resolve allegations of non-compliance with the law and curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and pursue our strategy. If any of the physicians or other healthcare providers or entities with whom we expect to do business, including future collaborators, are found not to be in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from participation in government healthcare programs, which could also affect our business.

Future legislation, and/or regulations and policies adopted by the FDA, the EMA or comparable regulatory authorities, may increase the time and cost required for us or our collaborators to conduct and complete clinical trials of our current and future product candidates.

The FDA and the EMA have each established regulations to govern the product development and approval process, as have other foreign regulatory authorities. The policies of the FDA, the EMA and other regulatory authorities may change. For example, in December 2016, the 21st Century Cures Act, or Cures Act, was signed into law. The Cures Act, among other things, is intended to modernize the regulation of drugs and spur innovation, but not all its provisions have yet been implemented. Additionally, in August 2017, the FDA issued final guidance setting forth its current thinking with respect to development programs and clinical trial designs for antibacterial drugs to treat serious bacterial diseases in patients with an unmet medical need. We cannot predict what if any effect the Cures Act or any existing or future guidance from the FDA or other regulatory authorities will have on the development of our product candidates.

Recently enacted and future legislation, including relevant provisions of the Inflation Reduction Act, may increase the difficulty and cost for us and our collaborators to obtain marketing approval of and commercialize our product candidates and affect the prices we may obtain.

In the United States and some foreign jurisdictions, there have been several legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and affect our ability to profitably sell any product candidates for which we obtain marketing approval.

Among policy makers and payors in the United States and elsewhere, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs, improving quality and/or expanding access.

Other federal health reform measures have been proposed and adopted in the United States. For example, the Medicare Access and CHIP Reauthorization Act of 2015 ended the use of the statutory formula for clinician payment and established a quality payment incentive program, also referred to as the Quality Payment Program. This program provides clinicians with two ways to participate, including through the Advanced Alternative Payment Models, or APMs, and the Merit-based Incentive Payment System, or MIPS. In November 2019, CMS issued a final rule finalizing the changes to the Quality Payment Program. It is unclear how payment reductions

or the introduction of the Quality Payment Program will impact overall physician reimbursement under the Medicare program. It is also unclear if changes in Medicare payments to providers would impact such providers' willingness to prescribe and administer our products, if approved.

Further, there has been heightened governmental scrutiny over the way companies set prices for their marketed products. For example, there have been several recent Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and patient programs, and reform government program reimbursement methodologies for drug products. In particular, the recently passed Inflation Reduction Act contains provisions designed to limit the prices paid by Medicare for various prescription drugs.

We expect that the ACA, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we receive for any approved product. Any reduction in reimbursement from Medicare or other government programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us or our collaborators from being able to generate revenue, attain profitability, or commercialize our drugs.

Legislative and regulatory proposals have been made to expand post-approval requirements and restrict sales and promotional activities for drugs. We cannot be sure whether additional legislative changes will be enacted, or whether the FDA regulations, guidance or interpretations will be changed, or what the impact of such changes on the marketing approvals of our product candidates, if any, may be. In addition, increased scrutiny by the U.S. Congress of the FDA's approval process may significantly delay or prevent marketing approval, as well as subject us to more stringent product labeling and post-marketing testing and other requirements.

Our product candidates may be subject to government price controls that may affect our revenue.

There has been heightened governmental scrutiny in the United States and abroad of pharmaceutical pricing practices considering the rising cost of prescription drugs and biologics. In the United States, such scrutiny has resulted in several recent Congressional inquiries and proposed and enacted federal legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for products. At the federal level, the former Trump Administration's budget proposal for fiscal year 2020 contained further drug price control measures that could be enacted during the 2020 budget process or in other future legislation, including, for example, measures to permit Medicare Part D plans to negotiate the price of certain drugs under Medicare Part B, to allow some states to negotiate drug prices under Medicaid, and to eliminate cost sharing for generic drugs for low-income patients. The former Trump Administration also released a "Blueprint", or plan, to lower drug prices and reduce out-of-pocket costs of drugs that contains additional proposals to increase drug manufacturer competition, increase the negotiating power of certain federal healthcare programs, incentivize manufacturers to lower the list price of their products, and reduce the out-of-pocket costs of drug products paid by consumers.

HHS has solicited feedback on some of these measures and has implemented others under its existing authority. For example, in May 2019, CMS issued a final rule to allow Medicare Advantage plans the option to use step therapy for Part B drugs beginning January 1, 2020. This final rule codified CMS's policy change that was effective January 1, 2019. On November 20, 2020, CMS issued an interim final rule through the CMS Innovation Center whereby Medicare Part B reimbursement for "certain high-cost prescriptions drugs" would be no more than most-favored-nation price (i.e., the lowest price) after adjustments, for a pharmaceutical product that the drug manufacturer sells in a member country of the Organization for Economic Cooperation and Development that has a comparable per-capita gross domestic product. On December 28, 2020, the United States District Court in Northern California issued a nationwide preliminary injunction against implementation of the interim final rule. While some of these and other measures may require additional authorization to become effective, members of Congress and the new Biden Administration have indicated that they will continue to seek new legislative and/or administrative measures to control drug costs. For example, the recently enacted Inflation Reduction Act contains provisions designed to limit the prices paid by Medicare for various prescription drugs. At the state level, legislatures have become increasingly aggressive in passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing.

Outside of the United States, particularly in the European Union, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. To obtain coverage and reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of our product candidate to other available therapies. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be harmed.

Risks Related to our Alliance with GSK

Because a portion of our current revenues and near-term projected revenues have historically been derived from products under the GSK Agreements, disputes with GSK could harm our business and cause the price of our securities to fall.

Historically, all of our current and near-term projected revenues have been derived from products under the GSK Agreements. We expect royalties from such products will likely continue to comprise a portion of our revenues in the future. Any action or inaction by either GSK or us that results in a material dispute, allegation of breach, litigation, arbitration, or significant disagreement between the parties may be interpreted negatively by the market or by our investors, could harm our business and cause the price of our securities to fall. Examples of these kinds of issues include but are not limited to non-performance of contractual obligations and allegations of non-performance, disagreements over the relative marketing and sales efforts for our partnered products and other GSK respiratory products, disputes over public statements, and similar matters.

Because GSK is a strategic partner, it may take actions that in certain cases are materially harmful to our business or to our stockholders.

GSK is a strategic partner with rights and obligations under the GSK Agreements that cause its interests to differ from our interests and those of our stockholders. In particular, GSK has a substantial respiratory product portfolio in addition to the partnered products that are covered by the GSK Agreements. GSK may make respiratory product portfolio decisions or statements about its portfolio which may be, or may be perceived to be, harmful to the respiratory products partnered with us. For example, GSK could promote its non-GSK/Innoviva respiratory products or a partnered product for which we are entitled to receive a lower percentage of royalties, delay or terminate the development or commercialization of the respiratory programs covered by the GSK Agreements, or take other actions, such as making public statements, that have a negative effect on our stock price. In this regard and by way of example, sales of Advair®, GSK's approved medicine for both COPD and asthma, continue to be significantly greater than sales of RELVAR®/BREO® ELLIPTA®, and GSK has indicated publicly that it intends to continue commercializing Advair®. Also, given the potential future royalty payments which GSK may be obligated to pay under the GSK Agreements, GSK may seek to acquire us in order to reduce those payment obligations. The timing of when GSK may seek to acquire us could potentially be when it possesses information regarding the status of drug programs covered by the GSK Agreements that has not been publicly disclosed and is not otherwise known to us. As a result of these differing interests, GSK may take actions that it believes are in its best interest but which might not be in our best interest or the best interest of our stockholders.

GSK has also indicated to us that it believes its consent may be required before we can engage in certain royalty monetization transactions with third parties, which may inhibit our ability to engage in these transactions.

GSK indicated to us that it believes that its consent may be required before we can engage in certain transactions designed to monetize the future value of royalties that may be payable to us from GSK under the GSK Agreements. GSK has informed us that it believes that there may be certain covenants included in these types of transactions that might violate certain provisions of the GSK Agreements. Although we believe that we can structure royalty monetization transactions in a manner that fully complies with the requirements of the GSK Agreements without GSK's consent, a third party in a proposed monetization transaction may nonetheless insist that we obtain GSK's consent for the transaction or restructure the transaction on less favorable terms. We have obtained GSK's agreement that (i) we may grant certain pre-agreed covenants in connection with monetization of our interests in RELVAR®/BREO® ELLIPTA®, ANORO® ELLIPTA® and vilanterol monotherapy, and (ii) it will not unreasonably withhold its consent to our requests to grant other covenants, provided among other conditions, that in each case, the covenants are not granted in favor of a pharmaceutical or biotechnology company with a product either being developed or commercialized for the treatment of respiratory disease. If we seek GSK's consent to grant covenants other than pre-agreed covenants, we may not be able to obtain GSK's consent on reasonable terms, or at all. If we proceed with a royalty monetization transaction that is not otherwise covered by the GSK Agreement without GSK's consent, GSK could request that its consent be obtained or seek to enjoin or otherwise challenge the transaction as violating or allowing it to terminate the GSK Agreements. Regardless of the merit of any claims by GSK, we would incur significant cost and diversion of resources in defending against GSK's claims or asserting our own claims and GSK may seek concessions from us in order to provide its consent. Any uncertainty about whether or when we could engage in a royalty monetization transaction, the potential impact on the enforceability of the GSK Agreements or the loss of potential royalties from the respiratory programs partnered with GSK, could impair our ability to pursue a return of capital strategy for our stockholders ahead of our receipt of significant royalties from GSK, result in significant reduction in the market price of our securities and cause other material harm to our business.

General Risks Factors

Our internal computer systems, or third-parties that we work with, may fail or suffer security breaches, which could result in a material disruption of our business.

Despite the implementation of security measures, our internal computer systems and those of third-parties with whom we work (including our collaborative partner) are vulnerable to damage or disruption from computer viruses, software bugs, unauthorized access, natural disasters, terrorism, war, and telecommunication, equipment and electrical failures. In the event we or they were to experience any significant system failure, accident or security breach it could cause interruptions in our operations and adversely affect our business, financial condition and results of operations. Cybersecurity attacks in particular are evolving and include, but are not limited to, malicious software, attempts to gain unauthorized access to data and other electronic security breaches that could lead to disruptions in systems, misappropriation of our confidential, or otherwise protected, information and corruption of data.

Additionally, California recently enacted legislation that has been dubbed the first "GDPR-like" law in the United States. Known as the California Consumer Privacy Act ("CCPA"), it creates new individual privacy rights for consumers (as that word is broadly defined in the law) and places increased privacy and security obligations on entities handling personal data of consumers or households. Having gone into effect January 1, 2020, the CCPA requires covered companies to provide new disclosures to California consumers, provide such consumers new ways to opt-out of certain sales of personal information, and allow for a new cause of action for data breaches. The CCPA may significantly impact our business activities and require substantial compliance costs that adversely affect business, operating results, prospects and financial condition.

Thus, any access, disclosure or other loss of information, including our data being breached at our partners or third-party providers, could result in legal claims or proceedings and liability under laws that protect the privacy of personal information, disrupt our operations and damage our reputation, which could adversely affect our business.

If we fail to maintain proper and effective internal control over financial reporting or if the interpretations, estimates or judgments utilized in preparing our financial statements prove to be incorrect, our operating results and our ability to operate our business could be harmed.

The Sarbanes-Oxley Act requires, among other things, that we establish and maintain effective internal control over financial reporting and disclosure controls and procedures. Under the SEC's current rules, we are required to perform system and process evaluation and testing of our internal control over financial reporting to allow management to report on the effectiveness of our internal control over financial reporting, as required by Section 404 of the Sarbanes-Oxley Act. Our independent registered public accounting firm is also required to report on our internal control over financial reporting. Our testing and our independent registered public accounting firm's testing may reveal deficiencies in our internal control over financial reporting that are deemed to be material weaknesses and render our internal control over financial reporting ineffective. We have and expect to continue to incur substantial accounting and auditing expense and to expend significant management time in complying with the requirements of Section 404. If we are not able to maintain compliance with the requirements of Section 404 in a timely manner, or if we or our independent registered public accounting firm identify deficiencies in our internal control over financial reporting that are deemed to be material weaknesses, the market price of our stock could decline and we could be subject to investigations or sanctions by the SEC, FINRA, The Nasdaq Global Select Market or other regulatory authorities. In addition, we could be required to expend significant management time and financial resources to correct any material weaknesses that may be identified or to respond to any regulatory investigations or proceedings.

We are also subject to complex tax laws, regulations, accounting principles and interpretations thereof. The preparation of our financial statements requires us to interpret accounting principles and guidance and make estimates and judgments that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the financial statements, as well as the reported revenue generated, and expenses incurred during the reporting periods. Our interpretations, estimates and judgments are based on our historical experience and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for the preparation of our financial statements. U.S. generally accepted accounting principles ("U.S. GAAP") presentation is subject to interpretation by the SEC, the Financial Accounting Standards Board and various other bodies formed to interpret and create appropriate accounting principles and guidance. In the event that one of these bodies disagrees with our accounting recognition, measurement or disclosure or any of our accounting interpretations, estimates or assumptions, it may have a significant effect on our reported results and may retroactively affect previously reported results. The need to restate our financial results could, among other potential adverse effects, result in our incurring substantial costs, affect our ability to timely file our periodic reports until such restatement is completed, divert the attention of our management and employees from managing our business, result in material changes to our historical and future financial results, result in investors losing confidence in our operating results, subject us to securities class action litigation, and cause our stock price to decline.

Our employees or third party providers, or employees or third party providers of our portfolio companies may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements and insider trading.

We are exposed to the risk of fraud or other misconduct by employees, third party providers, or employees or third party providers of our portfolio companies. Misconduct by employees, third party providers, or employees or third party providers of our portfolio companies could include intentional failures to comply with applicable regulations, provide accurate information to regulatory authorities, comply with federal and state fraud and abuse laws and regulations, report financial information or data accurately or disclose unauthorized activities to us. In particular, the health care industry is subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. It is not always possible to identify and deter misconduct by employees, third party providers, or employees or third party providers of our portfolio companies, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with these laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant fines or other sanctions.

We have incurred litigation and may incur additional litigation.

We have been subject to various legal proceedings, and, in the future, we may be exposed to, or threatened with, litigation, claims and proceedings incident to the ordinary course of, or otherwise in connection with, our business. In addition, agreements entered into by us sometimes include indemnification provisions which may subject us to costs and damages in the event of a claim against an indemnified third party.

Regardless of the merit of particular claims, litigation may be expensive, time-consuming, disruptive to our operations and distracting to management. In recognition of these considerations, we may enter into agreements or other arrangements to settle litigation and resolve such disputes. No assurance can be given that such agreements can be obtained on acceptable terms or that litigation will not occur. These agreements may also significantly increase our operating expenses.

If one or more legal matters were resolved against us or an indemnified third party in a reporting period for amounts in excess of management's expectations, our consolidated financial statements for that reporting period could be materially adversely affected. Further, such an outcome could result in significant compensatory, punitive or trebled monetary damages, disgorgement of revenue or profits, remedial corporate measures or injunctive relief against us that could materially adversely affect our financial condition and operating results.

While we maintain insurance coverage for certain types of claims, such insurance coverage may be insufficient to cover all losses or all types of claims that may arise.

Failure to comply with the U.S. Foreign Corrupt Practices Act, or "FCPA", as well as the anti-bribery laws of the nations in which we conduct business, could subject us to penalties and other adverse consequences.

We are subject to the FCPA, which generally prohibits U.S. companies from engaging in bribery or other prohibited payments to foreign officials for the purpose of obtaining or retaining business and requires companies to maintain accurate books and records and internal controls. In addition, we are subject to the anti-bribery laws of other jurisdictions in which we conduct business. Our employees or other agents may engage in prohibited conduct without our knowledge under our policies and procedures and the FCPA and other anti-bribery laws that we may be subject to for which we may be held responsible. If our employees or other agents are found to have engaged in such practices, we could suffer severe penalties and other consequences that may have a material adverse effect on our business, financial condition and results of operations.

U.S. federal income tax reform could adversely affect us.

On December 22, 2017, U.S. federal tax legislation, commonly referred to as the Tax Cuts and Jobs Act (TCJA), was signed into law, significantly reforming the U.S. Internal Revenue Code. The TCJA, among other things, includes changes to U.S. federal tax rates, imposes significant additional limitations on the deductibility of interest, allows for the expensing of capital expenditures, puts into effect the migration from a "worldwide" system of taxation to a territorial system and modifies or repeals many business deductions and credits.

The TCJA is a complex revision to the U.S. federal income tax laws with disparate and, in some cases, countervailing impacts on different categories of taxpayers and industries, and will require subsequent rulemaking and interpretation in a number of areas. The long-term impact of the TCJA on the overall economy, the industries in which we operate and our partners business cannot be reliably

predicted at this early stage of the new law's implementation. There can be no assurance that the TCJA will not negatively impact our operating results, financial condition, and future business operations. The estimated impact of the TCJA is based on our management's current knowledge and assumptions, following consultation with our tax advisors, and recognized impacts could be materially different from current estimates based on our actual results and our further analysis of the new law. The impact of the TCJA on holders of common stock is uncertain and could be materially adverse. This Annual Report does not discuss any such tax legislation or the manner in which it might affect investors in common stock. Investors should consult with their own tax advisors with respect to such legislation and the potential tax consequences of investing in common stock.

We are subject to evolving and complex tax laws, which may result in additional liabilities and affect our results of operations.

We are subject to income taxes in the U.S. and other jurisdictions, and in the course of our business, we make judgments about the expected tax treatment of various transactions and events. Changes in tax laws, regulations, administrative practices, principles, and interpretations, as well as events that differ from our expectations, have affected and may adversely affect our effective tax rates, cash flows, and/or results of operations. Significant uncertainty currently exists regarding tax proposals introduced by the U.S., including modifications to certain aspects of the Tax Cuts and Jobs Act of 2017, such as the potential repeal or deferral of the provision requiring capitalization of research and development expenses. In addition, tax authorities in the U.S. and other jurisdictions in which we do business routinely examine our tax returns and are intensifying their scrutiny and examinations of profit allocations among jurisdictions, which could unfavorably impact our results of operations. Further actions taken with respect to tax-related matters by associations such as the Organization for Economic Co-operation and Development and the European Commission could influence tax laws in countries in which we operate. Modifications to key elements of the current U.S. or international tax framework could have a significant impact on our effective tax rate, results of operations, and cash flows.

The widespread outbreak of an illness or any other communicable disease, or any other public health crisis, could adversely affect our business, results of operations and financial condition.

The outbreak of the novel coronavirus ("COVID-19") has negatively impacted the global economy, disrupted global supply chains, and created significant volatility and disruption of financial markets. The Company is closely monitoring developments related to the COVID-19 pandemic to assess its impact on the Company's business. It is possible that an extended period of global supply chain and economic disruption resulting from the COVID-19 pandemic could materially affect our results of operations and financial condition.

Under the Services Agreement with Sarissa Capital, we may rely on Sarissa Capital to assist in our strategic investing activity.

On December 11, 2020, we entered into the Services Agreement pursuant to which Sarissa Capital provides substantial assistance to us in connection with our acquisition strategy. Pursuant to the terms of the Services Agreement, and subject to the limitations set forth therein, Sarissa Capital will, among other things: (i) assist Innoviva in the development of an overall acquisition and investment process and strategy; (ii) advise Innoviva on market trends, market dynamics and merger and acquisition activity; (iii) identify potential transaction targets; (iv) assist in due diligence of transaction targets and the negotiation and execution of transactions; (v) advise on the growth and operational plans, performance and integration of target companies once an investment or acquisition is made; and (vi) assist in the identification of director and officer candidates for target companies. The services are provided by Sarissa Capital personnel and we have limited or no ability to control the manner upon which the services are provided. In the event that Sarissa Capital fails to adequately perform the required services, our investment activity operations and financial performance may be negatively impacted.

Our investment into the Partnership could subject us to various risks and uncertainties, any of which could impact our investment results and could materially and adversely affect our business, financial condition and results of operations.

Historically, we have invested our cash reserves in short-term investments and marketable securities, primarily corporate notes, government securities, government agencies, and commercial papers. On December 11, 2020, we entered into the Partnership Agreement and invested $300 million of our cash reserves to be managed by Sarissa Capital as the investment manager to the Partnership.

While we expect that a portion of our revenues will continue to be derived from our royalty management business, as a result of this investment, we may derive a material portion of our income from assets managed by Sarissa Capital. The investment strategy of Sarissa Capital will focus on a concentrated portfolio of "long" positions in publicly or privately traded securities (debt or equity) and derivatives of, and other financial instruments related to, each of the foregoing, specifically in the areas of healthcare, pharmaceuticals and biotechnology. The risks associated with this investment strategy may be substantially greater than the risks associated with traditional fixed-income investment strategies or other low-yield strategies.

We have limited rights to remove the general partner of the Partnership and do not have any right to participate in the management of the Partnership or the investment activity of Sarissa Capital. We are solely dependent on Sarissa Capital's management of our investment in the Partnership. We cannot provide assurance that Sarissa Capital will be successful in meeting our investment objectives. Unexpected market volatility or losses in the Partnership's securities portfolio could significantly and negatively affect our investment in the Partnership and therefore our investment results, financial condition or results of operations.

The Partnership Agreement limits our ability to withdraw our invested funds from the Partnership.

Under the terms of the Partnership Agreement, subject to limited exceptions, we are not entitled to withdraw our funds invested in the Partnership until expiration of a "lock-up" period. Following the expiration of the lock-up period, we are able to make annual withdrawals subject to 25% gating provision such that we would receive our entire account in the Partnership over four fiscal quarters. Therefore, we are limited in our ability to obtain liquidity with respect to those funds and are further subjects to market fluctuations with respect thereto, particularly given the expected concentrated nature of the Partnership's portfolio.

Sarissa Capital intends to continue to manage other third party capital and is not required to dedicate any minimum amount of time to the Partnership.

In addition to managing the Partnership, Sarissa Capital, its principals and their affiliates may engage in investment and trading activities for their own accounts and/or for the accounts of third parties and is not required to afford the Partnership exclusivity or priority with respect to investment or trading activities. Affiliates of Sarissa Capital manage and expect to continue to manage other client accounts which have objectives similar to the Partnership. The Partnership Agreement does not include any specific obligations or requirements concerning allocation of time, effort or investment opportunities to us or impose any restriction on the nature or timing of investments for accounts that Sarissa Capital or its affiliates may manage.

The price of our securities has been volatile and may continue to be so, and purchasers of our securities could incur substantial losses.

The price of our securities has been volatile and may continue to be so. Between January 1, 2022 and December 31, 2022, the high and low sales prices of our common stock as reported on The Nasdaq Global Select Market varied between $10.92 and $18.97 per share. The stock market in general and the market for biotechnology and biopharmaceutical companies in particular have experienced extreme volatility that has often been unrelated to the companies' operating performance, in particular during the last several years.

We may be unable to or elect not to return capital to our stockholders.

The payment of, or continuation of, capital returns to stockholders is at the discretion of our Board of Directors and is dependent upon our financial condition, results of operations, capital requirements, execution of our strategic initiatives, general business conditions, tax treatment of capital returns, potential future contractual restrictions contained in our credit agreement and other agreements and other factors deemed relevant by our Board of Directors. Future capital returns may also be affected by, among other factors: our views on potential future capital requirements for investments in acquisitions and our working capital and debt maintenance requirements; legal risks; stock or debt repurchase programs; changes in federal and state income tax laws or corporate laws; and changes to our business model. Our capital return programs may change from time to time, and we cannot provide assurance that we will continue to provide any particular amounts. Our announcement of future capital return programs does not obligate us to repurchase any specific dollar amount of debt or equity or number of shares of common stock. A reduction, suspension or change in our capital return programs could have a negative effect on our stock price.

Anti-takeover provisions in our charter and bylaws and in Delaware law could prevent or delay a change in control of our company.

Provisions of our Certificate of Incorporation and Bylaws may discourage, delay or prevent a merger or acquisition that stockholders may consider favorable, including transactions in which you might otherwise receive a premium for your shares. These provisions include:

- requiring supermajority stockholder voting to effect certain amendments to our Certificate of Incorporation and Bylaws;
- restricting the ability of stockholders to call special meetings of stockholders;
- prohibiting stockholder action by written consent; and

- establishing advance notice requirements for nominations for election to the board of directors or for proposing matters that can be acted on by stockholders at meetings.

In addition, some provisions of Delaware law may also discourage, delay or prevent someone from acquiring us or merging with us.

Unfavorable global economic and political conditions could adversely affect our business, financial condition or results of operations.

Our results of operations could be adversely affected by general conditions in the global economy, the global financial markets and the global political conditions. The United States and global economies are facing growing inflation, higher interest rates and potential recession. Portions of our future clinical trials may be conducted outside of the United States and unfavorable economic conditions resulting in the weakening of the United States dollar would make those clinical trials more costly to operate. Furthermore, a severe or prolonged economic downturn, including a recession or depression resulting from the current COVID-19 pandemic or political disruption such as the war between Ukraine and Russia could result in a variety of risks to our business, including weakened demand for our product candidates or any future product candidates, if approved, and our ability to raise additional capital when needed on acceptable terms, if at all. A weak or declining economy or political disruption, including any international trade disputes, could also strain our manufacturers or suppliers, possibly resulting in supply disruption, or cause our customers to delay making payments for our potential products. Any of the foregoing could seriously harm our business, and we cannot anticipate all of the ways in which the political or economic climate and financial market conditions could seriously harm our business.

The enactment of proposed or future tax legislation may adversely impact our financial condition and results of operations.

On August 16, 2022, President Biden signed the Inflation Reduction Act, or the IRA. The IRA contains a number of tax related provisions including a 15% minimum corporate income tax on certain large corporations as well as an exercise tax on stock repurchases, both provisions are effective for tax years beginning after December 31, 2022. We are in the process of evaluating the IRA to determine any impact on our financial condition and results of operations in the future.

ITEM 1B. UNRESOLVED STAFF COMMENTS

None.

ITEM 2. PROPERTIES

Our headquarters consist of a lease of 2,111 square feet of office space in Burlingame, California, which expires in December 2023. Our other material leased property is a combination of office space and laboratory facility of approximately 20,000 square feet located in Waltham, Massachusetts, which expires in December 2025. We also have a smaller rented facility in Waltham, Massachusetts. We believe that these facilities are sufficient for our current operational needs and that suitable additional space will be available on commercially reasonable terms to accommodate expansion of our operations, if necessary.

ITEM 3. LEGAL PROCEEDINGS

The information called for by this Item is incorporated herein by reference in Item 8. “Financial Statements and Supplementary Data,” Note 13. “Commitments and Contingencies”.

ITEM 4. MINE SAFETY DISCLOSURES

Not applicable.

PART II

ITEM 5. MARKET FOR REGISTRANT'S COMMON EQUITY, RELATED STOCKHOLDER MATTERS AND ISSUER PURCHASES OF EQUITY SECURITIES

Market Information

Our common stock was traded on Nasdaq under the symbol "THRX" from October 5, 2004 until January 8, 2016. Upon changing our corporate name to Innoviva, Inc. on January 7, 2016, we changed the stock ticker symbol to "INVA" effective January 11, 2016.

Holders

As of February 14, 2023, there were 64 stockholders of record of our common stock. As many of our shares of common stock are held by brokers and other institutions on behalf of stockholders, we are unable to estimate the total number of stockholders represented by these record holders.

Purchases of Equity Securities by the Issuer

The following table reflects share repurchases of our common stock for the three months ended December 31, 2022:

Period	Total Number of Shares Purchases	Average Price Paid per Share	Total Number of Shares Purchased as Part of Publicly Announced Plans or Programs [1]	Approximate Dollar Value of Shares That May Yet Be Purchased Under the Plans or Programs [1]
October 1, 2022 to October 31, 2022	—	$ —	—	$ —
November 1, 2022 to November 30, 2022	—	—	—	—
December 1, 2022 to December 31, 2022	647,394	13.13	647,394	91,496,562
Total	647,394	$ 13.13	647,394	$ 91,496,562

(1) On October 31, 2022, the Board of Directors of Innoviva authorized and approved a stock repurchase program pursuant to which we may purchase up to $100.0 million of our outstanding common stock. The timing and amount of any share repurchases under the share repurchase program will be determined by Innoviva's management in its discretion based on ongoing assessments of the capital needs of the business, the market price of Innoviva's common stock, prevailing stock prices, general market conditions and other considerations. Share repurchases under the program may be made through a variety of methods, which may include open market purchases, privately negotiated transactions, in block trades, accelerated share repurchase transactions, exchange transactions, or any combination thereof or by other means in accordance with federal securities laws. This program has no termination date, may be suspended or discontinued at any time at the Company's discretion and does not obligate the Company to acquire any amount of common stock.

Stock Performance Graph

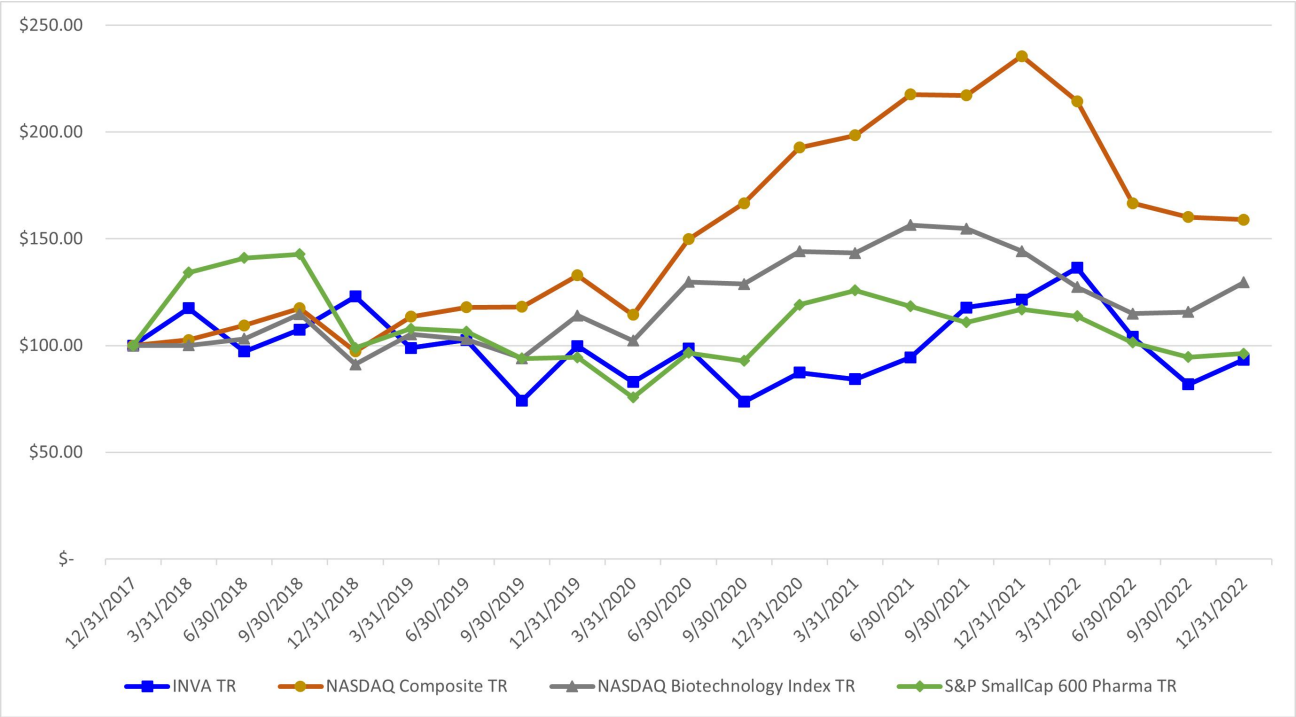
The graph set forth below compares the cumulative total stockholder return on our common stock for the period commencing on December 31, 2017 and ending on December 31, 2022, with the cumulative total return of (i) the Nasdaq Composite Index, (ii) the Nasdaq S&P Small Cap 600 Pharma Index and (iii) the Nasdaq Biotechnology Index over the same period. This graph assumes the investment of $100.00 on December 31, 2017 in each of (1) our common stock, (2) the Nasdaq Composite Index, (3) the Nasdaq S&P Small Cap 600 Pharma Index and (4) the Nasdaq Biotechnology Index, and assumes the reinvestment of dividends.

The comparisons shown in the graph below are based upon historical data. We caution that the stock price performance shown in the graph below is not necessarily indicative of, nor is it intended to forecast, the potential future performance of our common stock. Information used in the graph was obtained from sources believed to be reliable including Nasdaq, Bloomberg and Reuters, but we are not responsible for any errors or omissions in such information.

Notwithstanding anything to the contrary set forth in any of our previous or future filings under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended, that might incorporate this Annual Report on Form 10-K or future filings made by us under those statutes, this Stock Performance Graph section shall not be deemed filed with the SEC and shall not be deemed incorporated by reference into any of those prior filings or into any future filings made by us under those statutes.

COMPARISON OF 5 YEAR CUMULATIVE TOTAL RETURN*

Among Innoviva, Inc., the Nasdaq Composite Index, Nasdaq Biotechnology Index, and Nasdaq S&P Small Cap 600 Pharma Index.



* $100 invested on December 31, 2017 in stock or index, including reinvestment of dividends.

ITEM 6. [Reserved]

ITEM 7. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

Management's Discussion and Analysis ("MD&A") is intended to facilitate an understanding of our business and results of operations. This discussion and analysis should be read in conjunction with our consolidated financial statements and notes included in this Annual Report on Form 10-K. The information contained in this discussion and analysis or set forth elsewhere in this Annual Report on Form 10-K, including information with respect to our plans and strategy for our business, our operating expenses, and future payments under our collaboration agreements, includes forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. Such statements are based upon current expectations that involve risks and uncertainties. You should review the section entitled "Risk Factors" in Item 1A of Part I above for a discussion of important factors that could cause actual results to differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis. See the section entitled "Special Note Regarding Forward Looking Statements" above for more information.

Management Overview

Innoviva, Inc. (referred to as "Innoviva", the "Company", the "Registrant" or "we" and other similar pronouns) is a company with a portfolio of royalties and innovative healthcare assets. Our royalty portfolio contains respiratory assets partnered with Glaxo Group Limited ("GSK"), including RELVAR®/BREO® ELLIPTA® (fluticasone furoate/vilanterol, "FF/VI") and ANORO® ELLIPTA® (umeclidinium bromide/vilanterol, "UMEC/VI"), and up until July 2022, TRELEGY® ELLIPTA® (the combination FF/UMEC/VI). We sold our 15% ownership interest in Theravance Respiratory Company, LLC ("TRC") on July 20, 2022, and are no longer entitled to receive royalties on sales of TRELEGY® ELLIPTA® products. Under the Long-Acting Beta2 Agonist ("LABA") Collaboration Agreement, Innoviva is entitled to receive royalties from GSK on sales of RELVAR®/BREO® ELLIPTA® as follows: 15% on the first $3.0 billion of annual global net sales and 5% for all annual global net sales above $3.0 billion; and royalties from the sales of ANORO® ELLIPTA® which tier upward at a range from 6.5% to 10%.

We expanded our portfolio of royalties and innovative healthcare assets through the acquisition of Entasis Therapeutics Holdings Inc. ("Entasis") on July 11, 2022 and the acquisition of La Jolla Pharmaceutical Company ("La Jolla") on August 22, 2022. Following the acquisitions, our commercial and marketed products include GIAPREZA® (angiotensin II), approved to increase blood pressure in adults with septic or other distributive shock, and XERAVA® (eravacycline) for the treatment of complicated intra-abdominal infections in adults, and our development pipeline includes medicines for the treatment of bacterial infections, such as our lead asset sulbactam-durlobactam ("SUL-DUR"). As such, we have a wholly owned robust infectious disease and hospital operating platform as well as other assets in these therapeutic areas, such as a large equity stake in Armata Pharmaceuticals, a leader in bacteriophage development with potential use across a range of infectious and other serious diseases. We also have economic interests in other healthcare companies.

Our company structure and organization are tailored to our focused activities of managing our respiratory assets partnered with GSK, commercializing our marketed products, developing of our product candidates, optimizing capital allocation, and providing for certain essential reporting and management functions of a public company. As of December 31, 2022, we had 101 employees.

Financial Highlights

In the year ended December 31, 2022, the net income attributable to Innoviva stockholders was $213.9 million, a decrease of $52.0 million from net income attributable to Innoviva stockholders of $265.9 million in the year ended December 31, 2021. The lower net income was mainly driven by the decrease in fair values of equity and long-term investments, including $153.2 million in unrealized loss, and the decrease in our royalty revenues. These decreases were partially offset by a gain of $266.7 million recognized from the sale of TRC. Cash and cash equivalents totaled $291.0 million, and royalty and product sales receivable was $64.1 million as of December 31, 2022.

Corporate Updates

On July 11, 2022, we completed the purchase of all of the issued and outstanding equity securities of Entasis not already owned by Innoviva for $42.4 million in cash consideration. Entasis brings to Innoviva an infectious disease focused research and development platform anchored by its lead asset SUL-DUR.

On July 20, 2022, we completed the sale of our 15% ownership interest in TRC to Royalty Pharma Investments 2019 ICAV ("Royalty Pharma") for $282.0 million, including payment for our portion of TRC's cash balance of $4.4 million, and a potential $50.0 million sales-based milestone payments. We also received full ownership of equity and other investments that TRC owned prior to the transaction.

On August 22, 2022, we completed the acquisition of La Jolla for a net cash price of $150.5 million. La Jolla brings to Innoviva an established product portfolio, including GIAPREZA® (angiotensin II), approved to increase blood pressure in adults with septic or other distributive shock and XERAVA® (eravacycline) for the treatment of complicated intra-abdominal infections in adults.

On October 31, 2022, our Board of Directors authorized a new share repurchase program under which we may repurchase up to $100.0 million of Innoviva's outstanding shares of common stock. The timing and amount of any share repurchases under the share repurchase program will be determined by our management in its discretion based on ongoing assessments of the capital needs of the business, the market price of Innoviva's common stock, prevailing stock prices, general market conditions and other considerations. Share repurchases under the program may be made through a variety of methods, which may include open market purchases, privately negotiated transactions, in block trades, accelerated share repurchase transactions, exchange transactions, or any combination thereof or by other means in accordance with federal securities laws. This program has no termination date, may be suspended or discontinued at any time at our discretion and does not obligate us to acquire any amount of common stock. As of December 31, 2022, we have repurchased and retired 647,394 shares in the open market for total price of approximately $8.5 million. Subsequent to December 31, 2022 and through February 24, 2023, we have repurchased 1,522,947 shares in the open market for a total amount of approximately $19.2 million. All the repurchased shares were retired.

Clinical Updates

- On November 30, 2022, the U.S. Food and Drug Administration ("FDA") granted priority review for SUL-DUR, an investigational drug for the treatment of infections caused by Acinetobacter *baumannii-calcoaceticus* complex ("ABC"), including multi-drug resistant and carbapenem-resistant strains.
- The FDA is currently planning to hold an advisory committee meeting to discuss this New Drug Application. The target PDUFA date (or action date) is May 29, 2023.
- At the annual meeting of the Infectious Disease Society of America which took place from October 19 to October 23, 2022 in Washington, D.C., Entasis Therapeutics, a wholly owned subsidiary of the Company, had six presentations on SUL-DUR, reinforcing the positive safety and efficacy findings from the Company's pivotal Phase 3 ATTACK trial.
- Additionally, at the same annual meeting of the Infectious Disease Society of America, La Jolla Pharmaceutical, another wholly owned subsidiary of the Company, had five abstracts on XERAVA® focused primarily on its use in combination therapies.
- Enrollment in the phase 3 registrational trial for zoliflodacin, a first-in-class oral antibiotic for the treatment of gonorrhea being developed in partnership with GARD-P, remains on track, and study completion is anticipated in 2023.

Collaborative Arrangements with GSK

LABA Collaboration

In November 2002, we entered into the LABA Collaboration Agreement with GSK to develop and commercialize once-daily LABA products for the treatment of chronic obstructive pulmonary disorder ("COPD") and asthma (the "LABA Collaboration Agreement"). For the treatment of COPD, the collaboration has developed three combination products:

- RELVAR®/BREO® ELLIPTA® ("FF/VI") (BREO® ELLIPTA® is the proprietary name in the U.S. and Canada and RELVAR® ELLIPTA® is the proprietary name outside the U.S. and Canada), a once-daily combination medicine consisting of a LABA, vilanterol (VI), and an inhaled corticosteroid ("ICS"), fluticasone furoate ("FF"),
- ANORO® ELLIPTA® ("UMEC/VI"), a once-daily medicine combining a long-acting muscarinic antagonist ("LAMA"), umeclidinium bromide ("UMEC"), with a LABA, vilanterol (VI), and
- TRELEGY® ELLIPTA® (the combination FF/UMEC/VI), a once-daily combination medicine consisting of an ICS, LAMA and LABA.

As a result of the launch and approval of RELVAR®/BREO® ELLIPTA® and ANORO® ELLIPTA® in the U.S., Japan and Europe, in accordance with the LABA Collaboration Agreement, we paid milestone fees to GSK totaling $220.0 million during the year ended December 31, 2014. Although we have no further milestone payment obligations to GSK pursuant to the LABA Collaboration Agreement, we continue to have ongoing commercialization activities under the LABA Collaboration Agreement, including participation in the joint steering committee that are expected to continue over the life of the agreement. The milestone fees paid to GSK were recognized as capitalized fees paid, which are being amortized over their estimated useful lives commencing upon the commercial launch of the products.

We are entitled to receive royalties from GSK on sales of RELVAR®/BREO® ELLIPTA® as follows: 15% on the first $3.0 billion of annual global net sales and 5% for all annual global net sales above $3.0 billion. On sales of ANORO® ELLIPTA®, royalties are upward tiering and range from 6.5% to 10%. We no longer receive royalties on sales of TRELEGY® ELLIPTA® after we sold our royalty rights along with the sale of our ownership in TRC in July 2022.

Strategic Partnership with Sarissa Capital

Strategic Advisory Agreement

On December 11, 2020, we entered into a Strategic Advisory Agreement (the "Services Agreement") with Sarissa Capital Management LP ("Sarissa Capital"), pursuant to which Sarissa Capital provides a variety of strategic services to us in order to assist us in the development and execution of our acquisition strategy. The services are provided free of charge to us. Sarissa Capital is considered to be a related party due to its investment in Innoviva's common stock and its representation on our board of directors.

Partnership Agreement

On December 11, 2020, Innoviva Strategic Partners LLC ("Strategic Partners"), our wholly owned subsidiary, entered into a subscription agreement (the "Subscription Agreement") and an Amended and Restated Limited Partnership Agreement (the "Partnership Agreement") pursuant to which Strategic Partners became a limited partner of ISP Fund LP (the "Partnership"). The general partner of the Partnership (the "General Partner") is an affiliate of Sarissa Capital and, pursuant to an investment management agreement, Sarissa Capital acts as the investment adviser to the Partnership. Strategic Partners made a $300.0 million initial contribution into the Partnership. The Partnership was formed for the purposes of investing in equity securities in the healthcare, pharmaceutical and biotechnology industries. The Partnership Agreement provides for Sarissa Capital to receive a customary one percent management fee from the Partnership, payable quarterly in advance, measured based on the Net Asset Value of Strategic Partners' capital account in the Partnership. In addition, the General Partner is entitled to a customary 10% annual performance allocation based on the Net Profits of the Partnership during the annual measurement period. The Partnership Agreement includes a lock-up period of thirty-six months after which Strategic Partners is entitled to make withdrawals from the Partnership as of such lock-up expiration date and each anniversary thereafter, subject to certain limitations.

In May 2021, Strategic Partners received a distribution of $110.0 million from the Partnership to provide funding to Innoviva for a strategic repurchase of Innoviva common shares held by GSK. On March 30, 2022, Strategic Partners made an additional capital contribution of $110.0 million to the Partnership pursuant to the letter agreement entered into between Strategic Partners, the Partnership and Sarissa Capital Fund GP LP on May 20, 2021. The capital contribution is subject to a 36-month lock up period from the contribution date.

Critical Accounting Policies and Estimates

Our management's discussion and analysis of our financial condition and results of operations is based on our financial statements, which have been prepared in accordance with U.S. GAAP. The preparation of these financial statements requires us to make estimates and assumptions that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities as of the date of the financial statements, as well as the reported revenue generated and expenses incurred during the reporting periods. Our estimates are based on our historical experience and on various other factors that we believe are reasonable under the circumstances, the results of which form the basis for making judgments about the carrying value of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions. We believe that the accounting policies discussed below are critical to understanding our historical and future performance, as these policies relate to the more significant areas involving management's judgments and estimates.

Business Combinations

We use the acquisition method of accounting under Accounting Standards Codification ("ASC") Topic 805, *Business Combinations*. Each acquired company's operating results are included in our consolidated financial statements starting on the acquisition date. The purchase price is equivalent to the fair value of consideration transferred. Tangible and identifiable intangible assets acquired, liabilities assumed and any noncontrolling interest in the acquiree as of the acquisition date are recorded at the acquisition date fair value. Goodwill is recognized for the excess of purchase price over the net fair value of assets acquired and liabilities assumed.

Amounts allocated to assets and liabilities are based upon fair values. Such valuations require us to make significant estimates and assumptions, especially with respect to the identifiable intangible assets. We make estimates of fair value based upon assumptions believed to be reasonable and that of a market participant. Significant estimates and assumptions may involve projected future revenues, earnings, cash flows, estimated probabilities of certain milestone achievements, discount rates, asset lives, among other items. Our estimates may also impact our deferred tax assets and liabilities. Unanticipated events and circumstances may occur that may affect the accuracy and validity of such assumptions, estimates or actual results. Our estimates are based on available historical information as well as future expectations, and the estimates are inherently uncertain. The separately identifiable intangible assets generally include marketed products, in-process research and development and collaboration agreement.

Revenue Recognition from Royalties

We recognize the royalty revenue on net sales of products with respect to which we have contractual royalty rights in the period in which the royalties are earned. The net sales reports provided by our partner are based on its methodology and assumptions to estimate rebates and returns, which it monitors and adjusts regularly in light of contractual and legal obligations, historical trends, past experience and projected market conditions. Our partner may make significant adjustments to its sales based on actual results recorded, which could cause our royalty revenue to fluctuate. We conduct periodic royalty audits to evaluate the information provided by our partner. Royalties are recognized net of amortization of capitalized fees associated with any approval and launch milestone payments made to GSK.

Revenue Recognition from Product Sales

We started recognizing revenue from product sales as a result of our acquisition of La Jolla. We apply the guidance on principal versus agent considerations under ASC Topic 606, *Revenue from Contracts with Customers*, to determine the appropriate treatment for the transactions between us and third parties. The classification of transactions under our arrangements is determined based on the nature and contractual terms of the arrangement along with the nature of the operations of the participants. Any consideration related to activities in which we are considered the principal, which includes being in control of the good or service before such good or service is transferred to the customer, are accounted for as product sales.

Prior to recognizing any revenue from product sales, we identify the contract, performance obligations, and transaction price, and allocate the transaction price to the performance obligations. Revenue from product sales is recognized when our customers obtain control of the product and is recorded at the transaction price, net of estimates for variable consideration consisting of chargebacks, discounts, returns and rebates. Variable consideration is estimated using the expected-value amount method, which is the sum of probability-weighted amounts in a range of possible consideration amounts. Actual amounts of consideration ultimately received may differ from our estimates. If actual results vary materially from our estimates, we will adjust these estimates, which will affect revenue from product sales and earnings in the period such estimates are adjusted. These items may include:

- Chargebacks: Chargebacks are discounts we provide to distributors in the event that the sales prices to end users are below the distributors' acquisition price. This may occur due to a direct contract with a health system, a group purchasing organization ("GPO") agreement or a sale to a government facility. Chargebacks are estimated based on known chargeback rates and recorded as a reduction of revenue on delivery to our customers.
- Discounts: We offer customers various forms of incentives and consideration, including prompt-pay and other discounts. We estimate discounts primarily based on contractual terms. These discounts are recorded as a reduction of revenue on delivery to our customers.
- Returns: We offer customers a limited right of return, generally for damaged or expired product. We estimate returns based on an internal analysis, which includes actual experience. The estimates for returns are recorded as a reduction of revenue on delivery to our customers.
- Rebates: We participate in Medicaid rebate programs, which provide assistance to certain low-income patients based on each individual state's guidelines regarding eligibility and services. Under the Medicaid rebate programs, we pay a rebate to each participating state, generally within three months after the quarter in which product was sold. Additionally, we may offer customer incentives and consideration in the form of volume-based or other rebates. The estimates for rebates are recorded as a reduction of revenue on delivery to our customers.

We continue to assess our estimates of variable consideration as we accumulate additional historical data and will adjust these estimates accordingly.

Capitalized Fees Paid

We review our Capitalized Fees for impairment on a product-by-product basis for each major geographic area when events or changes in circumstances indicate that the carrying amount of such assets may not be recoverable. The recoverability of Capitalized Fees is measured by comparing the asset's carrying amount to the expected undiscounted future cash flows that the asset is expected to generate. The determination of recoverability typically requires various estimates and assumptions, including estimating the useful life over which cash flows will occur, their amount, and the asset's residual value, if any. We derive the required cash flow estimates from near-term forecasted product sales and long-term projected sales in the corresponding market. Based upon our analyses of past, current and future sales and trends, there have been no indicators of impairment and no impairment charges have been recorded on the Capitalized Fees as of December 31, 2022.

Variable Interest Entities

The primary beneficiary of a variable interest entity ("VIE') is required to consolidate the assets and liabilities of the VIE. When we obtain a variable interest in another entity, we assess at the inception of the relationship and upon occurrence of certain significant events whether the entity is a VIE and, if so, whether we are the primary beneficiary of the VIE based on our power to direct the activities of the VIE that most significantly impact the VIE's economic performance and our obligation to absorb losses or the right to receive benefits from the VIE that could potentially be significant to the VIE. To determine whether a variable interest that we hold could potentially be significant to the VIE, we consider both qualitative and quantitative factors regarding the nature, size and form of our involvement with the VIE.

To assess whether we have the power to direct the activities of a VIE that most significantly impact the VIE's economic performance, we consider all the facts and circumstances, including our role in establishing the VIE and our ongoing rights and responsibilities. This assessment includes identifying the activities that most significantly impact the VIE's economic performance and identifying which party, if any, has power over those activities. In general, the parties that make the most significant decisions affecting the VIE (management and representation on the Board of Directors) and have the right to unilaterally remove those decision-makers are deemed to have the power to direct the activities of a VIE.

To assess whether we have the obligation to absorb losses of the VIE or the right to receive benefits from the VIE that could potentially be significant to the VIE, we consider all of our economic interests that are deemed to be variable interests in the VIE. This assessment requires us to apply judgment in determining whether these interests, in the aggregate, are considered potentially significant to the VIE.

Equity and Long-Term Investments

We hold Series C preferred stock and preferred stock warrants in InCarda Therapeutics Inc. ("InCarda"), a privately held, clinical-stage biopharmaceutical company. The Series C preferred stock and warrants are classified as Level 3 financial instruments and recorded at fair value subject to remeasurement at each balance sheet date. We use the Black-Scholes-Merton pricing model to estimate the fair value of the warrants with the following input assumptions: the exercise price of the warrants, the risk-free interest rate computed based on the U.S. Treasury yield, the remaining contractual term as the expected term, and the expected stock price volatility calculated based on the historical volatility of the common stock of its public peer companies.

Our other Level 3 financial instruments include the Gate Neurosciences Inc. ("Gate") convertible promissory note and private placement positions held by ISP Fund LP as these securities are not publicly traded and the assumptions used in the valuation model for valuing these securities are based on significant unobservable and observable inputs including those of publicly traded peer companies. We measure the Gate convertible promissory note at fair value using a Monte Carlo simulation model with the probability of certain qualified events and the assumptions of equity value of Gate, risk-free rate, expected stock price, volatility of its peer companies, and the time until a financing is raised. Valuations models applied for the private placement positions held by ISP Fund LP may include the Black-Scholes-Merton pricing model, the Monte Carlo simulation model and other applicable valuation models. Key assumptions involve inputs to the Black-Scholes-Merton pricing model, probability rates of certain events and scenarios applied in the Monte Carlo simulation model and discount rates, as appropriate. The Monte Carlo simulation model also incorporates assumptions made based on transaction details such as the security's stock price, the expected term, maturity, risk-free interest rates and dividend yield, as well as volatility.

Factors Affecting Comparability

Our historical financial condition and results of operations for the periods presented may not be comparable, either between periods or going forward due to the factors described below.

- Adoption of Accounting Standards Update ("ASU") 2020-06 effective January 1, 2022;
- Accounting consolidation of Entasis on February 17, 2022 and purchase of remaining noncontrolling interest in Entasis on July 11, 2022;
- Sale of our 15% ownership interest in TRC on July 20, 2022; and
- Acquisition of La Jolla on August 22, 2022.

Refer to Note 1, "Description of Operations and Summary of Significant Accounting Policies", to the Consolidated Financial Statements for more information related to the adoption of ASU 2020-06. Refer to Note 5, "Consolidated Entities and Acquisitions", to the Consolidated Financial Statements for more information related to our acquisitions of Entasis and La Jolla and the sale of our ownership interest in TRC.

Results of Operations

Net Revenue

Royalty Revenue

Total net revenue from GSK, as compared to the prior years, was as follows:

	Year Ended December 31,			Change			
				2022		2021	
(In thousands)	2022	2021	2020	$	%	$	%
Royalties - RELVAR/BREO	$ 215,034	$ 234,066	$ 221,536	$ (19,032)	(8)%	$ 12,530	6%
Royalties - ANORO	38,405	44,935	45,992	(6,530)	(15)%	(1,057)	(2)%
Royalties - TRELEGY	72,029	126,688	73,089	(54,659)	(43)%	53,599	73%
Total royalties	325,468	405,689	340,617	(80,221)	(20)%	65,072	19%
Less: amortization of capitalized fees paid	(13,823)	(13,823)	(13,823)	—	*	—	*
Royalty revenue	311,645	391,866	326,794	(80,221)	(20)%	65,072	20%
Strategic alliance - MABA program	—	—	10,000	—	*	(10,000)	*
Total net royalty revenue	$ 311,645	$ 391,866	$ 336,794	$ (80,221)	(20)%	$ 55,072	16%

* Not Meaningful

Total net revenue decreased to $311.6 million for the year ended December 31, 2022, compared to the year ended December 31, 2021. The decrease in total net royalty revenue was primarily due to the sale of our ownership interest in TRC, which received royalties stemming from sales of TRELEGY® ELLIPTA®. Royalties for RELVAR®/BREO® ELLIPTA® and ANORO® ELLIPTA® decreased due to pricing pressures in the U.S. market and foreign currency rate changes.

Total net revenue increased to $391.9 million for the year ended December 31, 2021, compared to the year ended December 31, 2020. Royalties for RELVAR®/BREO® ELLIPTA® increased due to favorable adjustments, increased patient adherence and continued volume growth in certain markets. ANORO® ELLIPTA® decreased slightly mainly due to the increasing pricing pressure in the U.S. Royalties for TRELEGY® ELLIPTA® were higher due to the continued growth in triple therapy class and expanded sales in new markets.

Net Product Sales

Net product sales we recognized from the date of acquisition of La Jolla, which occurred on August 22, 2022, to December 31, 2022 was $19.7 million, consisting of net sales of GIAPREZA® and XERAVA® for $14.2 million and $5.5 million, respectively. We derived approximately 96% of our net product sales for the same period from customers located in the U.S. and 4% for the rest of the world.

Research & Development

Research and development expenses, as compared to the prior year period, were as follows:

	Year Ended December 31,			Change			
				2022		2021	
(In thousands)	2022	2021	2020	$	%	$	%
Research and development	$ 41,432	$ 576	$ 1,788	$ 40,856	*	$ (1,212)	(68)%

* Not Meaningful

Research and development expenses consisted of the following:

	Year Ended December 31,			Change			
				2022		2021	
(In thousands)	2022	2021	2020	$	%	$	%
External services	$ 24,666	$ 576	$ 1,788	$ 24,090	*	$ (1,212)	(68)%
Compensation and related personnel costs	13,863	—	—	13,863	*	—	*
Facilities related	2,255	—	—	2,255	*	—	*
Other	648	—	—	648	*	—	*
Total research and development expense	$ 41,432	$ 576	$ 1,788	$ 40,856	*	$ (1,212)	(68)%

* Not Meaningful

Research and development expenses for the year ended December 31, 2022 were mainly attributable to Entasis' product development efforts for our lead product candidate, SUL-DUR. External services costs consist primarily of fees paid to consultants, contractors and contract manufacturing organizations.

Research and development expenses for the years ended December 31, 2021 and 2020 were attributable to the product development efforts of Pulmoquine Therapeutics Inc., which was dissolved at the end of 2021.

Selling, General & Administrative

Selling, general and administrative expenses, as compared to the prior years, were as follows:

	Year Ended December 31,			Change			
				2022		2021	
(In thousands)	2022	2021	2020	$	%	$	%
Selling, general and administrative	$ 63,538	$ 16,187	$ 13,883	$ 47,351	293%	$ 2,304	17%

Selling, general and administrative expenses increased by $47.4 million for the year ended December 31, 2022, compared to the year ended December 31, 2021, mainly attributable to the consolidation of Entasis' operating expenses starting February 17, 2022 and the consolidation of La Jolla's operating expenses starting August 22, 2022.

Selling, general and administrative expenses increased by $2.3 million for the year ended December 31, 2021, compared to the year ended December 31, 2020, mainly attributable to increased business development activities and higher legal expenses incurred for the arbitration between Theravance Biopharma, the Company and TRC. The legal costs for the years ended December 31, 2021 and 2020 were $3.3 million and $1.7 million, respectively.

Interest and Dividend Income and Other Expense, Net

Interest and dividend income and other expense, net, as compared to the prior years, were as follows:

	Year Ended December 31,			Change			
				2022		2021	
(In thousands)	2022	2021	2020	$	%	$	%
Interest and dividend income	$ (6,369)	$ (1,839)	$ (1,524)	$ (4,530)	246%	$ (315)	21%
Other expense, net	3,373	3,626	348	(253)	(7)%	3,278	*

* Not Meaningful

Interest and dividend income increased for the year ended December 31, 2022, compared to the year ended December 31, 2021, due to higher interest rates and higher average balances of our cash equivalents, money market funds and other interest-bearing investments. Other expense, net, primarily consisted of expenses incurred by ISP Fund LP.

Interest and dividend income increased for the year ended December 31, 2021, compared to the year ended December 31, 2020, primarily due to higher returns on investments, including those managed by ISP Fund LP.

Interest Expense

Interest expense, as compared to the prior years, was as follows:

	Year Ended December 31,			Change			
				2022		2021	
(In thousands)	2022	2021	2020	$	%	$	%
Interest expense	$ 15,789	$ 19,070	$ 18,331	$ (3,281)	(17)%	$ 739	4%

The change in interest expense for the year ended December 31, 2022, compared to the year ended December 31, 2021, was primarily due to the adoption of ASU 2020-06, which simplifies the accounting for convertible debt instruments. As a result of the adoption, the debt discount associated with the cash settlement feature of our convertible senior notes due 2025 (the "2025 Notes") was adjusted to zero as of January 1, 2022. Interest expense for the year ended December 31, 2022 included the contractual interest expense and the amortization of debt issuance costs for our convertible subordinated notes due 2023 (the "2023 Notes"), the 2025 Notes and our convertible senior notes due 2028 (the "2028 Notes"). Interest expense for the year ended December 31, 2021 included the amortization of debt discount in addition to the contractual interest expense and the amortization of debt issuance costs for our 2023 Notes and 2025 Notes. The decrease in interest expense as a result of the adoption of ASU 2020-06 was partially offset by a higher debt balance and interest expense incurred for the deferred royalty obligation from the acquisition of La Jolla.

Interest expense increased slightly for the year ended December 31, 2021, compared to the year ended December 31, 2020, due to more debt discount and issuance costs being recognized through amortization.

Loss on Debt Extinguishment

We recognized a loss of $20.7 million due to the total premium payment of $20.4 million and the write-off of $0.3 million debt issuance costs in connection with the repurchase of $144.8 million aggregate principal amount of our 2023 Notes in March 2022.

Gain on Sale of TRC

We recognized a net gain of $266.7 million due to the sale of our ownership interest in TRC to Royalty Pharma, consummated on July 20, 2022.

Changes in Fair Values of Equity Method Investments and Other Equity and Long-Term Investments

Changes in fair values of equity method investments, net, and other equity and long-term investments, net, as compared to the prior years, were as follows:

	Year Ended December 31,			Change			
				2022		2021	
(In thousands)	2022	2021	2020	$	%	$	%
Changes in fair values of equity method investments, net	$ 161,749	$ (84,392)	$ (49,511)	$ 246,141	(292)%	$ (34,881)	70%
Changes in fair values of other equity and long-term investments, net	$ (8,462)	$ (6,638)	$ (766)	$ (1,824)	27%	$ (5,872)	767%

The changes in fair values of equity method investments and other equity and long-term investments year over year reflect the realized gains and losses and net unrealized gains and losses in our strategic investments in Armata, InCarda, and Gate, and those investments managed by ISP Fund LP.

The changes in fair values of equity method investments are attributed mainly to changes in the fair value of our investments in Armata and Entasis. We recorded $152.5 million in unrealized losses, $78.7 million in unrealized gains and $19.0 million in unrealized gains associated with our Armata investments for the years ended December 31, 2022, 2021 and 2020, respectively. The unrealized gains or losses on our investments in Armata is driven primarily by the share price changes of its publicly traded security. The amounts for the years ended December 31, 2022, 2021 and 2020 also include $9.2 million in unrealized losses, $5.7 million in unrealized gains and $30.5 million in unrealized gains, respectively, we recorded from our then investments in Entasis. Refer to Note 6, "Equity and Long-Term Investments and Fair Value Measurements", to the Consolidated Financial Statements for more information.

The changes in fair values of other equity and long-term investments year over year reflect the realized gains and losses and net unrealized gains and losses in our strategic investments in InCarda, Gate, and those investments managed by ISP Fund LP.

Income Taxes

Income tax expense, net, as compared to the prior years, was as follows:

	Year Ended December 31,			Change			
				2022		2021	
(In thousands)	2022	2021	2020	$	%	$	%
Income tax expense, net	$ 66,687	$ 76,439	$ 60,431	$ (9,752)	(13)%	$ 16,008	26%

As of December 31, 2022, 2021 and 2020, we had net operating loss carryforwards for federal income taxes of $411.5 million, $92.9 million and $361.5 million, respectively. As of December 31, 2022, 2021 and 2020, we also had state net operating loss carryforwards of approximately $955.3 million, $648.6 million and $650.7 million, respectively, which will expire beginning 2029. As of December 31, 2022, 2021 and 2020, we had federal research and development tax credit carryforwards of nil, $42.1 million, and $43.6 million, respectively. As of December 31, 2022, we had state research and development tax credits of $33.3 million.

For the year ended December 31, 2022, 2021 and 2020, we recognized $66.7 million, $76.4 million and $60.4 million of income tax expense, respectively, mainly based on the taxable income generated during those years.

We had total unrecognized tax benefits of $16.3 million as of December 31, 2022. Our total unrecognized tax benefits as of December 31, 2021 and December 31, 2020 were $14.9 million and $15.2 million, respectively.

Utilization of net operating loss and tax credit carryforwards is subject to rules, provided by the Internal Revenue Code and similar state provisions, governing annual limitations tied to ownership changes. We conducted an analysis of the Company through December 31, 2022 to determine whether an ownership change had occurred since inception. The study concluded that it is more likely than not that the Company did not experience an ownership change during the testing period. However, notwithstanding the applicable annual limitations, we estimate that no portion of our net operating loss or credit carryforwards will expire before becoming available to reduce federal and state income tax liabilities. Annual limitations may result in expiration of net operating loss and tax credit carryforwards before some or all of such amounts have been utilized. If we undergo another ownership change, the utilization of the pre-ownership change net operating loss carryforwards or pre-ownership change tax attributes, such as research tax credits, to offset the post-ownership change income may be subject to an annual limitation, pursuant to Sections 382 and 383 of the Internal Revenue Code of 1986, as amended. Similar rules may apply under state tax laws.

As a result of the acquisition of Entasis, we conducted a study of Entasis' ownership changes and estimated that we will be able to utilize $157.4 million of its federal net operating losses, which are subject to annual limitations.

As a result of the acquisition of La Jolla, we also performed a preliminary analysis of its ownership changes and estimated that we will be able to utilize $254.0 million of its federal net operating losses, which are subject to annual limitations.

Net Income Attributable to Noncontrolling Interests

Net income attributable to noncontrolling interests, as compared to the prior years, was as follows:

	Year Ended December 31,			Change			
				2022		2021	
(In thousands)	2022[(1)]	2021	2020	$	%	$	%
Net income attributable to noncontrolling interest	$ 6,341	$ 102,983	$ 69,412	$ (96,642)	(94)%	$ 33,571	48%

(1) The year ended December 31, 2022 represents the period from the initial date of consolidation of Entasis on February 17, 2022 to the date of the acquisition of Entasis on July 11, 2022, and the period from January 1, 2022 through the date of the sale of our ownership interest in TRC on July 20, 2022.

Net income attributable to noncontrolling interests for the year ended December 31, 2022 was $6.3 million compared to $103.0 million, a decrease of $96.6 million, which was mainly due to lower net income attributable to the sale of our ownership interest in TRC, offset with net loss attributable to Entasis' noncontrolling interest.

Net income attributable to noncontrolling interests during the years ended December 31, 2021 and 2020 represents the 85% share of net income in Theravance Respiratory Company, LLC for Theravance Biopharma. The year over year increase from 2020 to 2021 was primarily due to the growth in prescriptions and market share for TRELEGY® ELLIPTA®.

Liquidity and Capital Resources

Liquidity

Since our inception, we have financed our operations primarily through private placements and public offerings of equity and debt securities and payments received under collaborative arrangements. For the year ended December 31, 2022, we generated gross royalty revenues of $325.5 million and net product sales revenues of $19.7 million. Cash and cash equivalents totaled $291.0 million, royalties receivable from GSK totaled $54.7 million and accounts receivable associated with our product sales totaled $9.4 million, as of December 31, 2022.

As of December 31, 2022, we had three outstanding convertible notes, the 2023 Notes, the 2025 Notes and the 2028 Notes, in an aggregate principal amount of $549.7 million, of which $96.2 million matured and was fully paid in January 2023. The remainder amounts of $192.5 million and $261.0 million will become due in August 2025 and March 2028, respectively. Future interest payments associated with these notes total $46.0 million.

On October 31, 2022, our Board of Directors authorized a new share repurchase program under which we may repurchase up to $100.0 million of Innoviva's outstanding shares of common stock. As of December 31, 2022, we have repurchased Innoviva common stock in the open market for total price of approximately $8.5 million. This program has no termination date, may be suspended or discontinued at any time at our discretion and does not obligate us to acquire any amount of common stock.

In May 2021, Strategic Partners received a distribution of $110.0 million from the Partnership to provide funding to Innoviva for a strategic repurchase of Innoviva common shares held by GSK. On March 30, 2022, Strategic Partners made an additional capital contribution of $110.0 million to the Partnership pursuant to the letter agreement entered into between Strategic Partners, the Partnership and Sarissa Capital Fund GP LP on May 20, 2021. The capital contributions will then be subject to a 36-month lock up period from the contribution date.

Adequacy of Cash Resources to Meet Future Needs

We believe that our cash and cash equivalents will be sufficient to meet our anticipated debt service and operating needs, as well our ongoing share repurchase program, for at least the next 12 months based upon current operating plans and financial forecasts. Our long-term capital requirements will depend on many factors including the amount of our royalty revenues, sales growth of our currently marketed products, timing of regulatory approval of our product candidates and outcome of our acquisitions and strategic investments. If our current operating plans and financial forecasts change, we may require additional funding sooner in the form of public or private equity offerings or debt financings. Furthermore, if in our view favorable financing opportunities arise, we may seek additional funding in the form of public or private equity offerings or debt financings at any time. However, future financing may not be available in amounts or on terms acceptable to us, if at all. This could leave us without adequate financial resources to fund our operations as currently planned. In addition, from time to time we may restructure or reduce our debt, including through privately negotiated repurchases, tender offers, redemptions, amendments, or otherwise, all allowable with the terms of our debt agreements.

Cash Flows

Cash flows, as compared to the prior years, were as follows:

	Year Ended December 31,			Change	
(In thousands)	2022	2021	2020	2022	2021
Net cash provided by operating activities	$ 201,726	$ 363,813	$ 313,113	$ (162,087)	$ 50,700
Net cash provided by (used in) investing activities	(56,634)	43,722	(314,937)	(100,356)	358,659
Net cash used in financing activities	(55,568)	(452,497)	(29,785)	396,929	(422,712)

Cash Flows from Operating Activities

Cash provided by operating activities for the year ended December 31, 2022 was $201.7 million, consisting primarily of our net income of $220.3 million and net changes in operating assets and liabilities of $6.9 million, partially offset by net non-cash items of $25.4 million. Non-cash items included a net gain of $266.7 million recognized on the sale of TRC, partially offset by total non-cash charges of $241.3 million. Non-cash charges included a $153.3 million net decrease in fair values of equity method investments and other equity and long-term investments, $25.0 of deferred income taxes, $13.9 million of amortization of capitalized fees and depreciation of property and equipment and $5.6 million in amortization of acquired intangible assets, $20.7 million in loss on the extinguishment of debt, $7.3 million in stock-based compensation expense, $10.0 million in inventory fair value adjustments included in cost of products sold and $2.1 million in the amortization of debt discount and issuance costs. The changes in operating assets and liabilities included an increase in prepaid expenses of $21.4 million, a decrease in receivables from collaboration arrangements of $13.3 million and increases of $11.9 million and $10.0 million in accrued personnel-related expenses and other accrued liabilities and in income tax payable, respectively.

Cash provided by operating activities for the year ended December 31, 2021 was $363.8 million, consisting primarily of our net income of $368.8 million, adjusted for non-cash items such as $76.4 million of deferred income taxes, $13.8 million of depreciation and amortization, $9.1 million amortization of debt discount and issuance costs, $2.0 million of stock-based compensation expense, partially offset by a $89.3 million net increase in fair values of equity method investments and other equity and long-term investments and an increase in receivables from collaborative arrangements of $16.8 million.

Cash provided by operating activities for the year ended December 31, 2020 was $313.1 million, consisting primarily of our net income of $293.8 million, adjusted for non-cash items such as $60.4 million of deferred income taxes, $13.8 million of depreciation and amortization, $8.4 million amortization of debt discount and issuance costs, $1.7 million of stock-based compensation expense, partially offset by a $50.3 million increase in fair values of equity method investments and other equity and long-term investments and an increase in receivables from collaborative arrangements of $14.5 million.

Cash Flows from Investing Activities

Net cash used in investing activities for the year ended December 31, 2022 of $56.6 million included $159.1 million in cash paid for the acquisition of La Jolla, net of cash acquired, $58.7 million in purchases of equity and long-term investments, $60.9 million in purchases of equity investments managed by ISP Fund LP, $50.0 million in purchases of a trading security managed by ISP Fund LP and $23.4 million in net purchases and sales of other investments managed by ISP Fund LP. Net cash used in investing activities was partially offset by $248.2 million in net proceeds from the sale of our ownership interest in TRC, $24.3 million in sales of equity investments managed by ISP Fund LP and $23.1 million in cash acquired through the consolidation of Entasis.

Net cash provided by investing activities for the year ended December 31, 2021 of $43.7 million was primarily due to $110.0 million net cash inflow from $301.0 million sales and $191.0 million purchases of equity and other investments managed by ISP Fund LP, offset by $66.3 million in purchases of various investment instruments including, but not limited to, common stock, warrants, convertible debt investment, money market funds and other securities.

Net cash used in investing activities for the year ended December 31, 2020 of $314.9 million was primarily due to $300.0 million in the purchases of equity and other investments managed by ISP Fund LP and $100.9 million in purchases of common stock, warrants, money market funds, and other securities, offset by $86.0 million of proceeds received from maturities of marketable securities.

Cash Flows from Financing Activities

Net cash used in financing activities for the year ended December 31, 2022 of $55.6 million included $165.1 million for the repurchase of convertible subordinated notes due 2023, $69.8 million in distributions to noncontrolling interest, $43.9 million for the purchase of Entasis noncontrolling interest, $21.0 million for purchases of capped call options associated with our 2028 Notes and $8.5 million for the repurchase of common stock. Net cash used in financing activities was partially offset by $252.5 million in net proceeds from the issuance of our 2028 Notes.

Net cash used in financing activities for the year ended December 31, 2021 of $452.5 million was primarily due to a $394.1 million repurchase of our common stock from GSK and $59.5 million in distributions to noncontrolling interest.

Net cash used in financing activities for the year ended December 31, 2020 of $29.8 million was primarily due to $30.5 million distributions to noncontrolling interest.

Contractual Obligations

In March 2022, we completed a private placement of $261.0 million aggregate principal amount of unsecured convertible senior notes, the 2028 Notes, which will mature on March 15, 2028. Under the terms of the 2028 Notes, we will make interest payments of approximately 2.125% of outstanding principal. The principal balance of $261.0 million will become due in March 2028. As of December 31, 2022, our notes payable obligation also included $96.2 million related to our 2023 Notes, which matured and was fully paid in January 2023 and $192.5 million related to our 2025 Notes which are due in 2025. Under the term of the 2025 Notes, we will make interest payments of 2.5% of outstanding principal. Refer to Note 12, "Debt" to the Consolidated Financial Statements for more information.

Our short-term and long-term obligations also include contractual payments related to our operating leases amounting to $4.1 million, with approximately $1.5 million payable through December 31, 2023 and approximately $1.3 million payable in each of the years 2024 and 2025. Refer to Note 13, "Commitments and Contingencies" to the Consolidated Financial Statements for more information.

As part of our acquisition of La Jolla, we recognized its deferred royalty obligation in connection with La Jolla Royalty Agreement with HCR. Under the terms of the Agreement, HCR is entitled to receive quarterly royalties on worldwide net sales of GIAPREZA® until either January 1, 2031 or when the maximum aggregate royalty payments have been made, whichever occurs first. Quarterly payments to HCR under the Royalty Agreement start at a maximum royalty rate, with step-downs based on the achievement of annual net product sales thresholds. The current maximum royalty rate is 14%. Starting January 1, 2024, the maximum royalty rate may increase by an additional 4%, if an agreed-upon, cumulative net product sales threshold has not been met. The La Jolla Royalty Agreement is subject to maximum aggregate royalty payments to HCR of $225.0 million.

Additionally, we have certain contingent payment obligations under various in-license agreements which we are required to make royalty payments or milestone payments upon successful completion and achievement of certain milestones. Refer to Note 4, "License and Collaboration Arrangements" to the Consolidated Financial Statements for more information.

We also enter into agreements in the normal course of business with vendors for manufacturing, clinical trials and preclinical studies, and other services and products for operating purposes.

ITEM 7A. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

As of December 31, 2022, our debt bears fixed interest rates and we had no outstanding debt with variable interest rates. Our cash flows on these debt obligations are not subject to variability as a result of changes in interest rates.

We are exposed to changes in the fair value of certain of our investments in equity and debt securities. Fluctuations in the underlying fair value of the investments could result in material gains or losses. Refer to Note 6 "Equity and Long-Term Investments and Fair Value Measurements" to the Consolidated Financial Statements for more information.

Inflation has increased during the period covered by this Annual Report on Form 10-K and could continue to increase for the near future. Inflationary factors, such as increases in the cost of our raw materials, supplies, interest rates and overhead costs may adversely affect our operating results. Although we do not believe that inflation has had a material impact on our financial position or results of operations to date, we may experience some effect in the near future if inflation rates continue to rise. Significant adverse changes in inflation and prices in the future could result in material losses.

We may face foreign exchange risk as a result of entering into transactions denominated in currencies other than U.S. dollars, including contracts with international vendors related to raw material purchases. Our royalty revenue from RELVAR®/BREO® ELLIPTA® and ANORO® ELLIPTA® is also indirectly exposed to foreign exchange risk as GSK also markets and sells the products outside the U.S. The majority of our cash and cash equivalents, investments, and the majority of our vendor relationships are denominated in U.S. dollars. Therefore, we do not believe that the risk of a significant impact on our operating income from foreign currency fluctuations is substantial.

ITEM 8. FINANCIAL STATEMENTS AND SUPPLEMENTARY DATA

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INNOVIVA, INC.

CONSOLIDATED BALANCE SHEETS

(In thousands, except per share data)

	December 31, 2022	December 31, 2021
Assets		
Current assets:		
Cash and cash equivalents	$ 291,049	$ 201,525
Accounts receivable	9,401	—
Receivables from collaboration arrangements	54,672	110,711
Inventory	55,897	—
Prepaid expenses	29,559	1,367
Other current assets	2,933	70
Total current assets	443,511	313,673
Property and equipment, net	170	12
Equity and long-term investments	403,013	483,845
Capitalized fees paid, net	97,607	111,430
Right-of-use assets	3,265	97
Goodwill	26,713	—
Intangible assets	252,919	—
Deferred tax assets, net	—	17,327
Other assets	4,299	11
Total assets	$ 1,231,497	$ 926,395
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$ 2,939	$ 27
Accrued personnel-related expenses	8,022	619
Accrued interest payable	4,359	4,152
Deferred revenue	2,094	—
Convertible subordinated notes due 2023, net of issuance costs	96,193	—
Income tax payable	154	—
Other accrued liabilities	21,207	1,009
Total current liabilities	134,968	5,807
Long-term debt, net of discount and issuance costs	444,180	394,653
Other long-term liabilities	70,918	—
Deferred tax liabilities, net	5,771	—
Income tax payable, long-term	9,872	—
Commitments and contingencies (Note 13)		
Stockholders' equity:		
Preferred stock: $0.01 par value, 230 shares authorized, no shares issued and outstanding	—	—
Common stock: $0.01 par value, 200,000 shares authorized, 69,188 and 69,566 issued and outstanding as of December 31, 2022 and December 31, 2021 respectively	692	696
Treasury stock: at cost, 32,005 shares as of December 31, 2022 and December 31, 2021	(393,829)	(393,829)
Additional paid-in capital	1,163,836	1,264,024
Accumulated deficit	(204,911)	(456,148)
Total Innoviva stockholders' equity	565,788	414,743
Noncontrolling interests	—	111,192
Total stockholders' equity	565,788	525,935
Total liabilities and stockholders' equity	$ 1,231,497	$ 926,395

See accompanying notes to consolidated financial statements.

INNOVIVA, INC.
CONSOLIDATED STATEMENTS OF INCOME
(In thousands, except per share data)

	Year Ended December 31,		
	2022	2021	2020
Revenue:			
Royalty revenue from a related party, net of amortization of capitalized fees paid of $13,823 in each of the years ended December 31, 2022, 2021 and 2020	$ 311,645	$ 391,866	$ 326,794
Revenue from collaborative arrangement	—	—	10,000
Net product sales	19,694	—	—
Total revenue	331,339	391,866	336,794
Expenses:			
Cost of products sold (inclusive of amortization of inventory fair value adjustments and excluding amortization of acquired intangible assets)	13,793	—	—
Selling, general and administrative	63,538	16,187	13,883
Research and development	41,432	576	1,788
Amortization of acquired intangible assets	5,581	—	—
Gain on sale of Theravance Respiratory Company, LLC (“TRC”)	(266,696)	—	—
Loss on extinguishment of debt	20,662	—	—
Changes in fair values of equity method investments, net	161,749	(84,392)	(49,511)
Changes in fair value of other equity and long-term investments, net	(8,462)	(6,638)	(766)
Interest and dividend income	(6,369)	(1,839)	(1,524)
Interest expense	15,789	19,070	18,331
Other expense, net	3,373	3,626	348
Total expenses	44,390	(53,410)	(17,451)
Income before income taxes	286,949	445,276	354,245
Income tax expense, net	66,687	76,439	60,431
Net income	220,262	368,837	293,814
Net income attributable to noncontrolling interests	6,341	102,983	69,412
Net income attributable to Innoviva stockholders	$ 213,921	$ 265,854	$ 224,402
Basic net income per share attributable to Innoviva stockholders	$ 3.07	$ 3.24	$ 2.21
Diluted net income per share attributable to Innoviva stockholders	$ 2.37	$ 2.87	$ 2.02
Shares used to compute Innoviva basic and diluted net income per share:			
Shares used to compute basic net income per share	69,644	82,062	101,320
Shares used to compute diluted net income per share	95,248	94,310	113,554

See accompanying notes to consolidated financial statements.

INNOVIVA, INC.
CONSOLIDATED STATEMENTS OF COMPREHENSIVE INCOME
(In thousands)

	Year Ended December 31,		
	2022	2021	2020
Net income	$ 220,262	$ 368,837	$ 293,814
Reclassifications to net income	—	—	(27)
Comprehensive income	220,262	368,837	293,787
Comprehensive income attributable to noncontrolling interests	6,341	102,983	69,412
Comprehensive income attributable to Innoviva stockholders	$ 213,921	$ 265,854	$ 224,375

See accompanying notes to consolidated financial statements.

INNOVIVA, INC.
CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY
(In thousands)

	Common Stock		Additional Paid-In	Accumulated Other Comprehensive	Accumulated	Treasury Stock		Noncontrolling	Total Stockholders'
	Shares	Amount	Capital	Income (Loss)	Deficit	Shares	Amount	Interest	Equity
Balance as of January 1, 2020	101,288	$ 1,013	$ 1,258,859	$ 27	$ (946,404)	—	$ —	$ 28,621	342,116
Distributions to noncontrolling interests	—	—	—	—	—	—	—	(30,474)	(30,474)
Equity activity of noncontrolling interests in a consolidated variable interest entity	—	—	—	—	—	—	—	366	366
Exercise of stock options and issuance of common stock units and stock awards, net of repurchase of shares to satisfy tax withholding	104	1	343	—	—	—	—	—	344
Stock-based compensation	—	—	1,698	—	—	—	—	—	1,698
Net income	—	—	—	—	224,402	—	—	69,412	293,814
Other comprehensive income	—	—	—	(27)	—	—	—	—	(27)
Balance as of December 31, 2020	101,392	$ 1,014	$ 1,260,900	$ —	$ (722,002)	—	$ —	$ 67,925	$ 607,837
Distributions to noncontrolling interests	—	—	—	—	—	—	—	(59,457)	(59,457)
Equity activity of noncontrolling interests in a consolidated variable interest entity	—	—	—	—	—	—	—	(259)	(259)
Exercise of stock options and issuance of common stock units and stock awards, net of repurchase of shares to satisfy tax withholding	179	2	1,107	—	—	—	—	—	1,109
Repurchase of common stock	(32,005)	(320)	—	—	—	32,005	(393,829)	—	(394,149)
Stock-based compensation	—	—	2,017	—	—	—	—	—	2,017
Net income	—	—	—	—	265,854	—	—	102,983	368,837
Balance as of December 31, 2021	69,566	$ 696	$ 1,264,024	$ —	$ (456,148)	32,005	$ (393,829)	$ 111,192	$ 525,935
Cumulative adjustment due to adoption of ASU 2020-06	—	—	(65,467)	—	37,238	—	—	—	(28,229)
Distributions to noncontrolling interests	—					—	—	(69,811)	(69,811)
Recognition of noncontrolling interest upon initial consolidation of Entasis	—	—	—	—	—	—	—	38,471	38,471
Equity activity of noncontrolling interests in a consolidated variable interest entity						—	—	(2)	(2)
Derecognition of noncontrolling interests upon sale of TRC	—	—	—	—	78	—	—	(61,304)	(61,226)
Derecognition of noncontrolling interests upon acquisition of Entasis noncontrolling interest	—	—	(14,153)	—	—	—	—	(28,009)	(42,162)
Exercise of stock options and issuance of common stock units and stock awards, net of repurchase of shares to satisfy tax withholding	269	2	286	—	—	—	—	—	288
Capped call options associated with convertible senior notes due 2028	—	—	(16,585)	—	—	—	—	—	(16,585)
Conversion of convertible subordinated notes due 2023	—	—	3	—	—	—	—	—	3
Repurchase of common stock	(647)	(6)	(8,497)	—	—			—	(8,503)
Stock-based compensation	—	—	4,225	—	—	—	—	3,122	7,347
Net income	—	—	—	—	213,921	—	—	6,341	220,262
Balance as of December 31, 2022	69,188	$ 692	$ 1,163,836	$ —	$ (204,911)	32,005	$ (393,829)	$ —	$ 565,788

See accompanying notes to consolidated financial statements.

INNOVIVA, INC.
CONSOLIDATED STATEMENTS OF CASH FLOWS
(In thousands)

	Year Ended December 31,		
	2022	2021	2020
Cash flows from operating activities			
Net income	$ 220,262	$ 368,837	$ 293,814
Adjustments to reconcile net income to net cash provided by operating activities:			
Deferred income taxes	25,006	76,432	60,420
Amortization of capitalized fees and depreciation of property and equipment	13,931	13,832	13,840
Amortization of acquired intangible assets	5,581	—	—
Fair value adjustments included in cost of products sold	10,023	—	—
Stock-based compensation	7,347	2,017	1,698
Amortization of debt discount and issuance costs	2,055	9,136	8,397
Changes in fair values of equity method investments, net	161,749	(84,392)	(49,511)
Changes in fair values of other equity and long-term investments, net	(8,462)	(4,917)	(766)
Loss on extinguishment of debt	20,662	—	—
Net gain on sale of TRC	(266,696)	—	—
Amortization of discount on short-term investments	—	—	(343)
Amortization of lease guarantee	—	—	(135)
Other non-cash items	3,402	(259)	21
Changes in operating assets and liabilities:			
Accounts receivable	(3,525)	—	—
Receivables from collaboration arrangements	13,319	(16,780)	(14,504)
Inventory	280	—	—
Prepaid expenses	(21,350)	203	(678)
Other assets	(3,341)	—	—
Accounts payable	92	(39)	56
Accrued personnel-related expenses and other accrued liabilities	11,913	(257)	804
Accrued interest payable	207	—	—
Deferred revenue	(755)	—	—
Income tax payable	10,026	—	—
Net cash provided by operating activities	201,726	363,813	313,113
Cash flows from investing activities			
Maturities of marketable securities	—	—	86,000
Purchases of marketable securities	—	—	(12,943)
Purchases of equity and long-term investments	(58,725)	(66,278)	(87,981)
Purchases of equity investments managed by ISP Fund LP	(60,910)	(190,970)	(14,877)
Purchases of trading security managed by ISP Fund LP	(50,000)	—	—
Sales of equity investments managed by ISP Fund LP	24,281	21,440	—
Purchase and sales of other investments managed by ISP Fund LP, net	(23,371)	279,530	(285,123)
Purchases of property and equipment	(67)	—	(13)
Proceeds from sale of ownership interest in TRC, net	248,191	—	—
Cash acquired through the consolidation of Entasis	23,070	—	—
Cash paid for the acquisition of La Jolla, net of cash acquired	(159,103)	—	—
Net cash provided by (used in) investing activities	(56,634)	43,722	(314,937)
Cash flows from financing activities			
Distributions to noncontrolling interests	(69,811)	(59,457)	(30,474)
Purchase of Entasis noncontrolling interest	(43,910)	—	—
Repurchase of common stock	(8,503)	(394,149)	—
Repurchase of shares to satisfy tax withholding	(82)	(60)	(92)
Proceeds from issuances of common stock	370	1,169	436
Net proceeds from the issuance of variable interest entity's equity	—	—	345
Payment for repurchase of convertible subordinated notes due 2023	(165,131)	—	—
Purchases of capped call options associated with convertible senior notes due 2028	(21,037)	—	—
Proceeds from issuance of convertible senior notes due 2028, net of issuance costs	252,536	—	—
Net cash used in financing activities	(55,568)	(452,497)	(29,785)
Net increase (decrease) in cash and cash equivalents	89,524	(44,962)	(31,609)
Cash and cash equivalents at beginning of period	201,525	246,487	278,096
Cash and cash equivalents at end of period	$ 291,049	$ 201,525	$ 246,487

	Year Ended December 31,		
	2022	2021	2020
Supplemental Disclosure of Cash Flow Information:			
Cash paid for interest	$ 11,736	$ 9,933	$ 9,933
Cash paid for income taxes	$ 53,855	$ —	$ —
Supplemental Disclosure of Non-cash Investing and Financing Activities:			
Adoption of ASU 2020-06	$ (28,228)	$ —	$ —

See accompanying notes to consolidated financial statements.

INNOVIVA, INC.
NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

1. DESCRIPTION OF OPERATIONS AND SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES

Description of Operations

Innoviva, Inc. (referred to as "Innoviva", the "Company", or "we" and other similar pronouns) is a company with a portfolio of royalties and innovative healthcare assets. Our royalty portfolio contains respiratory assets partnered with Glaxo Group Limited ("GSK"), including RELVAR®/BREO® ELLIPTA® (fluticasone furoate/vilanterol, "FF/VI") and ANORO® ELLIPTA® (umeclidinium bromide/vilanterol, "UMEC/VI"), and up until July 2022, TRELEGY® ELLIPTA® (the combination FF/UMEC/VI). We sold our 15% ownership interest in Theravance Respiratory Company, LLC ("TRC") on July 20, 2022, and are no longer entitled to receive royalties on sales of TRELEGY® ELLIPTA® products. Under the Long-Acting Beta2 Agonist ("LABA") Collaboration Agreement, Innoviva is entitled to receive royalties from GSK on sales of RELVAR®/BREO® ELLIPTA® as follows: 15% on the first $3.0 billion of annual global net sales and 5% for all annual global net sales above $3.0 billion; and royalties from the sales of ANORO® ELLIPTA®, which tier upward at a range from 6.5% to 10%.

We expanded our portfolio of royalties and innovative healthcare assets through the acquisition of Entasis Therapeutics Holdings Inc. ("Entasis") on July 11, 2022 and the acquisition of La Jolla Pharmaceutical Company ("La Jolla") on August 22, 2022. Our commercial and marketed products include GIAPREZA® (angiotensin II), approved to increase blood pressure in adults with septic or other distributive shock, and XERAVA® (eravacycline) for the treatment of complicated intra-abdominal infections in adults. Our development pipeline includes medicines for the treatment of bacterial infections, such as our lead asset sulbactam-durlobactam ("SUL-DUR"). As such, we have a wholly owned robust infectious disease and hospital operating platform, as well as other assets in these areas, such as a large equity stake in Armata Pharmaceuticals, a leader in bacteriophage development with potential use across a range of infectious and other serious diseases. We also have economic interests in other healthcare companies.

Principles of Consolidation

The accompanying consolidated financial statements include the accounts of Innoviva, our wholly owned subsidiaries and certain variable interest entities ("VIE") for which we are the primary beneficiary. All intercompany balances and transactions have been eliminated in consolidation. For consolidated entities where we own or are exposed to less than 100% of the economics, we record net income (loss) attributable to noncontrolling interest in our consolidated statements of income equal to the percentage of the economic or ownership interest retained in such entity by the respective noncontrolling party.

Presentation Reclassification

Certain amounts in prepaid expenses and other current assets, other assets and changes in fair values of equity and long-term investments, net, reported in the Company's prior year financial statements have been reclassified to conform to the current year presentation. These reclassifications had no net effect on the net income or net cash flows as previously reported.

Factors Affecting Comparability

Our historical financial condition and results of operations for the periods presented may not be comparable, either between periods or going forward due to the factors below and as discussed in Note 5, "Consolidated Entities and Acquisitions".

- Adoption of Accounting Standards Update ("ASU") 2020-06 effective January 1, 2022;
- Accounting consolidation of Entasis on February 17, 2022 and purchase of remaining noncontrolling interest in Entasis on July 11, 2022;
- Sale of our 15% ownership interest in TRC on July 20, 2022; and
- Acquisition of La Jolla on August 22, 2022.

Use of Management's Estimates

The preparation of consolidated financial statements in conformity with U.S. Generally Accepted Accounting Principles ("U.S. GAAP") requires management to make estimates and assumptions that affect the amounts reported in the consolidated financial statements and accompanying notes. Actual results could differ materially from those estimates. Management evaluates its significant accounting policies and estimates on an ongoing basis. We base our estimates on historical experience and other relevant assumptions that we believe to be reasonable under the circumstances. These estimates also form the basis for making judgments about the carrying values of assets and liabilities when these values are not readily apparent from other sources.

Concentrations of Credit Risk and of Significant Suppliers and Partners

Our financial instruments that are exposed to concentrations of credit risk consist primarily of cash and cash equivalents and equity and long-term investments. Although we deposit our cash with multiple financial institutions, our deposits, at times, may exceed federally insured limits.

We are dependent on third-party manufacturers to supply active pharmaceutical ingredients ("API") and drug products for research and development and commercial programs. These programs could be adversely affected by significant interruption in the supply of API or drug products.

Currently, we derive most of our revenues from GSK and our near-term success depends in large part on GSK's ability to successfully develop and commercialize the products in the respiratory programs partnered with GSK. Our near-term success depends in large part upon the performance by GSK of its commercial obligations under the GSK Agreements and the commercial success of RELVAR®/BREO® ELLIPTA® and ANORO® ELLIPTA®. If GSK does not devote sufficient resources to the commercialization or development of these products, is unsuccessful in its efforts, or chooses to reprioritize its commercial programs, our business would be materially harmed. GSK is responsible for all clinical and other product development, regulatory, manufacturing and commercialization activities for products developed under the GSK Agreements, including RELVAR®/BREO® ELLIPTA® and ANORO® ELLIPTA®. Our royalty revenues may fluctuate due to a variety of factors, many of which are outside of our control. Our royalty revenues under the GSK Agreements may not meet our, analysts' or investors' expectations, due to a number of important factors.

We also started recognizing revenue from product sales as a result of our acquisition of La Jolla Hospitals and other healthcare organizations generally purchase our products through a network of specialty distributors. These specialty distributors, which are located in the U.S., are considered our customers for accounting purposes. We do not believe that loss of one of these distributors would significantly impact our ability to distribute our products, as we expect that sales volume would be absorbed by new or remaining distributors. Three of our customers each account for 33%, 29% and 28%, respectively, of our net product sales from the time of our acquisition of La Jolla through December 31, 2022. These same customers account for 23%, 37% and 37%, respectively, of our receivables from net product sales, which are included in "Accounts receivables, net" on our consolidated balance sheet as of December 31, 2022.

Segment Reporting

We operate in a single segment, which is to provide capital return to stockholders by maximizing the potential value of our portfolio of royalties and innovative healthcare assets. Our Chief Operating Decision Maker ("CODM") is our Chief Executive Officer. The CODM allocates resources and evaluates the performance of Innoviva at the consolidated level using information about our revenues, operating results and other key financial data as needed. Our revenues are generated primarily from our collaborative arrangements and royalty payments from GSK, located in Great Britain. We also generate revenue from net sales of GIAPREZA® and XERAVA®. Refer to Note 3, "Revenue Recognition", for more information on our revenues for the periods presented. Our long-term assets are located within the United States.

Variable Interest Entities

The primary beneficiary of a variable interest entity ("VIE') is required to consolidate the assets and liabilities of the VIE. When we obtain a variable interest in another entity, we assess at the inception of the relationship and upon occurrence of certain significant events whether the entity is a VIE and, if so, whether we are the primary beneficiary of the VIE based on our power to direct the activities of the VIE that most significantly impact the VIE's economic performance and our obligation to absorb losses or the right to receive benefits from the VIE that could potentially be significant to the VIE.

To assess whether we have the power to direct the activities of a VIE that most significantly impact the VIE's economic performance, we consider all the facts and circumstances, including our role in establishing the VIE and our ongoing rights and responsibilities. This assessment includes identifying the activities that most significantly impact the VIE's economic performance and identifying which party, if any, has power over those activities. In general, the parties that make the most significant decisions

affecting the VIE (management and representation on the Board of Directors) and have the right to unilaterally remove those decision-makers are deemed to have the power to direct the activities of a VIE.

To assess whether we have the obligation to absorb losses of the VIE or the right to receive benefits from the VIE that could potentially be significant to the VIE, we consider all of our economic interests that are deemed to be variable interests in the VIE. This assessment requires us to apply judgment in determining whether these interests, in the aggregate, are considered potentially significant to the VIE.

Business Combination

When we acquire an entity in a business combination, we recognize the fair value of all assets acquired, liabilities assumed, and any non-controlling interest in the acquiree and establish the acquisition date as the fair value measurement point. We recognize and measure goodwill as of the acquisition date, as the excess of the fair value of the consideration paid over the fair value of the identified net assets acquired. Acquisition-related expenses and related restructuring costs are expensed as incurred.

Several valuation methods may be used to determine the fair value of assets acquired and liabilities assumed. For intangible assets, we typically use the income method. This method starts with a forecast of all of the expected future net cash flows for each asset. These cash flows are then adjusted to present value by applying an appropriate discount rate that reflects the risk factors associated with the cash flow streams. Some of the more significant estimates and assumptions inherent in the income method or other methods include the amount and timing of projected future cash flows, the discount rate selected to measure the risks inherent in the future cash flows and the assessment of the asset's life cycle and the competitive trends impacting the asset, including consideration of any technical, legal, regulatory, or economic barriers to entry. Determining the useful life of an intangible asset also requires judgment as different types of intangible assets will have different useful lives and certain assets may even be considered to have indefinite useful lives.

Cash and Cash Equivalents

We consider all highly liquid investments purchased with a maturity of three months or less on the date of purchase to be cash equivalents. Cash equivalents are carried at cost, which approximates fair value.

Investments in Marketable Securities

We invest in short-term investments and marketable securities, primarily corporate notes, government securities, government agencies, and government commercial papers. We limit the amount of credit exposure with any one issuer, industry or geographic area for investments other than instruments backed by the U.S. federal government. We classify our marketable securities as available-for-sale securities and report them at fair value in cash equivalents or short-term marketable securities on the consolidated balance sheets with related unrealized gains and losses included as a component of stockholders' equity. The amortized cost of debt securities is adjusted for amortization of premiums and accretion of discounts to maturity, which is included in interest income on the consolidated statements of operations. Realized gains and losses, if any, on available-for-sale securities are included in interest income. The cost of securities sold is based on the specific identification method. Interest and dividends on securities classified as available-for-sale are included in interest and dividend income.

We regularly review all of our investments for other-than-temporary declines in estimated fair value. Our review includes the consideration of the cause of the impairment, including the creditworthiness of the security issuers, the number of securities in an unrealized loss position, the severity and duration of the unrealized losses, whether we have the intent to sell the securities and whether it is more likely than not that we will be required to sell the securities before the recovery of their amortized cost basis. When we determine that the decline in estimated fair value of an investment is below the amortized cost basis and the decline is other-than-temporary, we reduce the carrying value of the security and record a loss for the amount of such decline to other expense, net.

Accounts Receivable

Accounts receivable are recorded net of estimates for prompt-pay discounts, chargebacks, returns and rebates. Allowances for prompt-pay discounts and chargebacks are based on contractual terms. We estimate the allowance for credit losses based on existing contractual payment terms, actual payment patterns of customers and individual customer circumstances.

Inventory

Inventory is stated at the lower of cost or estimated net realizable value on a first in, first out basis. We periodically analyze inventory levels and write down inventory as cost of products sold when the following occurs: inventory has become obsolete, inventory has a cost basis in excess of its estimated net realizable value, or inventory quantities are in excess of expected product sales.

Property and Equipment

Property and equipment, which consisted of laboratory equipment, computer equipment, software, office furniture and fixtures, and leasehold improvements, were not material as of December 31, 2022 and 2021, respectively.

Property and equipment are stated at cost less accumulated depreciation. Property and equipment are depreciated using the straight-line method as follows:

Leasehold improvements	Shorter of remaining lease terms or useful life
Laboratory equipment, furniture and fixtures	5 - 7 years
Software and computer equipment	3 years

Equity and Long-Term Investments

We invest from time to time in equity and debt securities of private or public companies. If we determine that we have control over these companies under either voting or VIE models, we consolidate them in our consolidated financial statements. If we determine that we do not have control over these companies under either voting or VIE models, we then determine if we have an ability to exercise significant influence via voting interests, board representation or other business relationships.

We may account for the investments where we exercise significant influence using either an equity method of accounting or at fair value by electing the fair value option under Accounting Standards Codification ("ASC") Topic 825, *Financial Instruments*. If the fair value option is applied to an investment that would otherwise be accounted for under the equity method, we apply it to all our financial interests in the same entity (equity and debt, including guarantees) that are eligible items. All gains and losses from fair value changes, unrealized and realized, are presented as changes in fair values of equity method investments, net, and changes in fair values of other equity and long-term investments, net, on the consolidated statements of income.

If we conclude that we do not have an ability to exercise significant influence over an investee, we may elect to account for the equity investment without a readily determinable fair value using the measurement alternative under ASC Topic 312, *Investments - Equity Securities*. This measurement alternative allows us to measure the equity investment at its cost minus impairment, if any, plus or minus changes resulting from observable price changes in orderly transactions for the identical or a similar investment of the same issuer.

We also invest in ISP Fund LP, which investments consist of money market funds, trading and equity securities in the healthcare, pharmaceutical and biotechnology industries. Pursuant to the Partnership Agreement entered in December 2020, we became a limited partner of this partnership, and our contributions are subject to a 36-month lock-up period which restriction prevents us to have control and access to the contributions and related investments. These investments are classified as long-term investments on the consolidated balance sheets.

Fair Value of Financial Instruments

We define fair value as the exchange price that would be received for an asset or paid to transfer a liability (an exit price) in the principal or most advantageous market for the asset or liability in an orderly transaction between market participants on the measurement date.

Our valuation techniques are based on observable and unobservable inputs. Observable inputs reflect readily obtainable data from independent sources, while unobservable inputs reflect our market assumptions. We classify these inputs into the following hierarchy:

Level 1—Quoted prices for identical instruments in active markets.

Level 2—Quoted prices for similar instruments in active markets; quoted prices for identical 3or similar instruments in markets that are not active; and model-derived valuations whose inputs are observable or whose significant value drivers are observable.

Level 3—Unobservable inputs and little, if any, market activity for the assets.

Financial instruments include cash equivalents, accounts receivable, receivables from collaborative arrangements, accounts payable, and accrued liabilities, equity investments and convertible promissory notes. The carrying values of cash equivalents, receivables from collaborative arrangements, accounts payable, and accrued liabilities approximate their estimated fair values due to the relatively short-term nature of these instruments.

Capitalized Fees Paid

We capitalize fees paid to licensors related to agreements for approved products or commercialized products. We capitalize these fees as capitalized fees paid ("Capitalized Fees") and amortize them on a straight-line basis over their estimated useful lives upon the commercial launch of the product, shortly after its regulatory approval. The estimated useful lives of these Capitalized Fees are determined on a country-by-country and product-by-product basis, as the later of the expiration or termination of the last patent right covering the compound in such product in such country and 15 years from first commercial sale of such product in such country, unless the Collaboration Agreement is terminated earlier. Consistent with our policy for classification of costs under the research and development collaborative arrangements, the amortization of these Capitalized Fees is recognized as a reduction of royalty revenue. We review our Capitalized Fees for impairment on a product-by-product basis for each major geographic area when events or changes in circumstances indicate that the carrying amount of such assets may not be recoverable. The recoverability of Capitalized Fees is measured by comparing the asset's carrying amount to the expected undiscounted future cash flows that the asset is expected to generate. The determination of recoverability typically requires various estimates and assumptions, including estimating the useful life over which cash flows will occur, their amount, and the asset's residual value, if any. We derive the required cash flow estimates from near-term forecasted product sales and long-term projected sales in the corresponding market.

Goodwill and Intangible Assets

Goodwill is recognized as the excess of the purchase consideration of an acquired entity over the fair value assigned to assets acquired and liabilities assumed in a business combination. Goodwill and intangible assets with indefinite useful life are not amortized and are tested for impairment at least annually on the first day of December of each year or more frequently if indicators for potential impairment exist or whenever events or changes in circumstances indicate that the asset's carrying asset amount may not be recoverable. Intangible assets with definite useful lives are amortized on a straight-line basis over their respective remaining useful lives and are tested for impairment only if indicators for potential impairment exist or whenever events or changes in circumstances indicate that the asset's carrying amount may not be recoverable. Significant judgment may be involved in determining if an indicator of impairment has occurred.

Operating Leases

Right-of-use assets represent our right to use an underlying asset over the lease term and include any lease payments made prior to the lease commencement date and are reduced by lease incentives. Lease liabilities represent the present value of the total lease payments over the lease term, calculated using an estimated incremental borrowing rate. Lease expense is recognized on a straight-line basis over the expected lease term.

Revenue Recognition

We apply the guidance on principal versus agent considerations under ASC Topic 606, *Revenue from Contracts with Customers*, to determine the appropriate treatment for the transactions between us and third parties. The classification of transactions under our arrangements is determined based on the nature and contractual terms of the arrangement along with the nature of the operations of the participants. Any consideration related to activities in which we are considered the principal, which includes being in control of the good or service before such good or service is transferred to the customer, are accounted for as product sales.

Revenue is recognized when our customer obtains control of promised goods or services, in an amount that reflects the consideration which we expect to receive in exchange for those goods or services. Revenue is recognized through a five-step process: (i) identify the contract with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price for the contract; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenue as a performance obligation is satisfied.

Royalty Revenue

We recognize the royalty revenue on net sales of products with respect to which we have contractual royalty rights in the period in which the royalties are earned. The net sales reports provided by our partner are based on its methodology and assumptions to estimate rebates and returns, which it monitors and adjusts regularly in light of contractual and legal obligations, historical trends, past experience and projected market conditions. Our partner may make significant adjustments to its sales based on actual results recorded, which could cause our royalty revenue to fluctuate. We conduct periodic royalty audits to evaluate the information provided by our partner. Royalties are recognized net of amortization of capitalized fees associated with any approval and launch milestone payments made to GSK.

Revenue from Product Sales

Revenue from product sales is recognized when our customers obtain control of the product and is recorded at the transaction price, net of estimates for variable consideration consisting of chargebacks, discounts, returns and rebates. Variable consideration is estimated using the expected-value amount method, which is the sum of probability-weighted amounts in a range of possible consideration amounts. Actual amounts of consideration ultimately received may differ from our estimates. If actual results vary materially from our estimates, we will adjust these estimates, which will affect revenue from product sales and earnings in the period such estimates are adjusted. These items may include:

- Chargebacks: Chargebacks are discounts we provide to distributors in the event that the sales prices to end users are below the distributors' acquisition price. This may occur due to a direct contract with a health system, a group purchasing organization ("GPO") agreement or a sale to a government facility. Chargebacks are estimated based on known chargeback rates and recorded as a reduction of revenue on delivery to our customers.
- Discounts: We offer customers various forms of incentives and consideration, including prompt-pay and other discounts. We estimate discounts primarily based on contractual terms. These discounts are recorded as a reduction of revenue on delivery to our customers.
- Returns: We offer customers a limited right of return, generally for damaged or expired product. We estimate returns based on an internal analysis, which includes actual experience. The estimates for returns are recorded as a reduction of revenue on delivery to our customers.
- Rebates: We participate in Medicaid rebate programs, which provide assistance to certain low-income patients based on each individual state's guidelines regarding eligibility and services. Under the Medicaid rebate programs, we pay a rebate to each participating state, generally within three months after the quarter in which product was sold. Additionally, we may offer customer incentives and consideration in the form of volume-based or other rebates. The estimates for rebates are recorded as a reduction of revenue on delivery to our customers.

We continue to assess our estimates of variable consideration as we accumulate additional historical data and will adjust these estimates accordingly.

Research and Development Expenses

Research and development expenses are recognized in the period that services are rendered or goods are received. Research and development expenses consist of salaries and benefits, laboratory supplies, facilities and other overhead costs, research-related manufacturing costs, contract service and clinical-related service costs performed by third party research organizations, research institutions and other outside service providers. Non-refundable prepayments for goods or services that will be used or rendered for future research and development activities are deferred and capitalized. Such amounts are recognized as an expense as the related goods are delivered or the related services are performed. We also utilize significant judgment and estimates to record accruals for estimated ongoing research expenses based on the progress of the studies and progress of research manufacturing activities.

Interest Expense on Deferred Royalty Obligation

Interest expense related to the deferred royalty obligation is recognized over the expected repayment term of the deferred royalty obligation using the effective interest method. The assumptions used in determining the expected repayment term of the deferred royalty obligation require us to make estimates that could impact the effective interest rate. Each reporting period, we estimate the expected repayment term of the deferred royalty obligation based on forecasted net sales of GIAPREZA®. Changes in interest expense resulting from changes in the effective interest rate, if any, are recorded on a prospective basis. Refer to Note 12, “Debt”, for more information.

Fair Value of Stock-Based Compensation Awards

We use the Black-Scholes-Merton option pricing model to estimate the fair value of options granted under our equity incentive plans and rights to acquire stock granted under our employee stock purchase plan (“ESPP”). The Black-Scholes-Merton option valuation model requires the use of assumptions, including the expected term of the award and the expected stock price volatility. We use the “simplified” method as described in Staff Accounting Bulletin No. 107, “*Share-Based Payment*,” for the expected option term. We use our historical volatility to estimate expected stock price volatility.

Restricted stock units (“RSUs”) and restricted stock awards (“RSAs”) are measured based on the fair market values of the underlying stock on the dates of grant.

Stock-based compensation expense is calculated based on awards ultimately expected to vest and is reduced for estimated forfeitures at the time of grant and revised, if necessary, in subsequent periods if actual forfeitures differed from those estimates. Our estimated annual forfeiture rates for stock options, RSUs and RSAs are based on our historical forfeiture experience.

The estimated fair value of stock options, RSUs and RSAs is expensed on a ratable or straight-line basis over the expected term of the grant or expected term of the vesting. Compensation expense is recorded over the requisite service period based on management’s best estimate as to whether it is probable that the shares awarded are expected to vest.

Compensation expense for purchases under the ESPP is recognized based on the fair value of the common stock on the date of offering, less the purchase discount percentage provided for in the plan.

Income Taxes

We utilize the asset and liability method of accounting for income taxes. Under this method, deferred tax assets and liabilities are determined based on differences between financial reporting and the tax basis of assets and liabilities and are measured using enacted tax rates and laws that will be in effect when the differences are expected to reverse. A valuation allowance is provided when it is more likely than not that some portion or all of a deferred tax asset will not be realized.

The recognition and measurement of tax benefits requires significant judgment. Our judgment might change as new information becomes available. We continue to evaluate our deferred tax assets each reporting period to determine whether adjustments to our valuation allowance are required and deferred tax assets will be realized based on the consideration of all available positive and negative evidence, including the differences between our anticipated and actual future operating results, using a “more likely than not” standard.

We assess all material positions taken in any income tax return, including all significant uncertain positions, in all tax years that are still subject to assessment or challenge by relevant taxing authorities. Assessing an uncertain tax position begins with the initial determination of the position's sustainability and is measured at the largest amount of benefit that is greater than 50% likely to be realized upon ultimate settlement. As of each balance sheet date, unresolved uncertain tax positions must be reassessed, and we determine whether the factors underlying the sustainability assertion have changed and whether the amount of the recognized tax benefit is still appropriate.

Comprehensive Income

Comprehensive income is comprised of net income and other comprehensive income (loss). Other comprehensive income (loss) consists of changes in unrealized and realized gains and losses on our marketable securities and the related tax impact of these changes.

Related Parties

Transactions with GSK were considered related party transactions up until May 2021, when we completed the share repurchase agreement with GSK to buy back all of its shares of common stock in Innoviva. GSK is no longer considered a related party after the completion of the share repurchase. Transactions with GSK are described in Note 3, "Revenue Recognition and Collaborative Arrangements."

Sarissa Capital owned 9.6% of our outstanding common stock as of December 31, 2022. Transactions with Sarissa Capital are described in Note 5, "Consolidated Entities and Acquisitions". Sarissa Capital is considered to be a related party because two of its principals are members of our board of directors.

Accounting Pronouncements Adopted by the Company

In August 2020, the FASB issued ASU 2020-06, *Debt-Debt with Conversion and Other Options (Subtopic 470-20) and Derivatives and Hedging-Contracts in Entity's Own Equity (Subtopic 815-40): Accounting for Convertible Instruments and Contracts in an Entity's Own Equity*, which is intended to simplify the accounting for convertible instruments by removing certain separation models in Subtopic 470-20 for convertible instruments. Consequently, a convertible debt instrument will be accounted for as a single liability measured at its amortized cost, as long as no other features require bifurcation and recognition as derivatives. The new standard also requires the if-converted method to be used to calculate diluted earnings per share ("EPS") for convertible instruments. Effective January 1, 2022, we adopted the new standard using the modified retrospective approach and assessed the effect of this adoption on the accounting for our outstanding convertible notes. The effect of the adoption on our 2025 Notes (as defined below) resulted in a decrease to the opening balance of accumulated deficit of $37.2 million, a reduction to additional paid-in capital of $65.4 million, an increase to the balance of the notes by an aggregate amount of $35.6 million, and an increase to deferred tax assets of $7.4 million. The dilutive EPS of our 2025 Notes will be computed under the if-converted method going forward. There was no financial impact from the implementation of the standard for our 2023 Notes (as defined below). Refer to Note 12, "Debt", for more information.

In October 2021, the FASB issued ASU 2021-08, *Business Combinations* (Topic 805), *Accounting for Contract Assets and Contract Liabilities from Contracts with Customers*, which requires contract assets and contract liabilities (i.e., deferred revenue) acquired in a business combination to be recognized and measured by the acquirer on the acquisition date in accordance with ASC Topic 606, *Revenue from Contracts with Customers*. During the third quarter of 2022, we elected to early adopt ASU 2021-08 effective July 1, 2022. The adoption did not have a material impact on our consolidated financial statements.

2. NET INCOME PER SHARE

Basic net income per share attributable to Innoviva stockholders is computed by dividing net income attributable to Innoviva stockholders by the weighted-average number of shares of common stock outstanding. Diluted net income per share attributable to Innoviva stockholders is computed by dividing net income attributable to Innoviva stockholders by the weighted-average number of shares of common stock and dilutive potential common stock equivalents then outstanding. Dilutive potential common stock equivalents include the assumed exercise, vesting and issuance of employee stock awards using the treasury stock method, as well as common stock issuable upon assumed conversion of our convertible subordinated notes due 2023 (the "2023 Notes"), our convertible senior notes due 2025 (the "2025 Notes"), and our convertible senior notes due 2028 (the "2028 Notes") using the if-converted method.

INNOVIVA, INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

The 2025 Notes are convertible, based on the applicable conversion rate, into cash, shares of our common stock or a combination thereof, at our election. Our current intent is to settle the principal amount of the 2025 Notes in cash upon conversion. The impact of the assumed conversion premium to diluted net income per share was historically computed using the treasury stock method until the adoption of ASU 2020-06. As the average market price per share of our common stock as reported on The Nasdaq Global Select Market was lower than the initial conversion price of $17.26 per share, there was no dilutive effect of the assumed conversion premium for the years ended December 31, 2021 and 2020 respectively. The dilutive EPS of the notes was $0.31 per share using the if-converted method for the year ended December 31, 2022 as a result of the adoption of ASU 2020-06.

The following table shows the computation of basic and diluted net income per share for the years ended December 31, 2022, 2021 and 2020:

	Year Ended December 31,		
(In thousands except per share data)	**2022**	**2021**	**2020**
Numerator:			
Net income attributable to Innoviva stockholders, basic	$ 213,921	$ 265,854	$ 224,402
Add: interest expense on 2023 Notes, net of tax effect	2,439	4,736	4,717
Add: interest expense on 2025 Notes, net of tax effect	4,583	—	—
Add: interest expense on 2028 Notes, net of tax effect	4,626	—	—
Net income attributable to Innoviva stockholders, diluted	$ 225,569	$ 270,590	$ 229,119
Denominator:			
Weighted-average shares used to compute basic net income per share attributable to Innoviva stockholders	69,644	82,062	101,320
Dilutive effect of 2023 Notes	6,188	12,189	12,189
Dilutive effect of 2025 Notes	11,150	—	—
Dilutive effect of 2028 Notes	8,158	—	—
Dilutive effect of options and awards granted under equity incentive plan and employee stock purchase plan	108	59	45
Weighted-average shares used to compute diluted net income per share attributable to Innoviva stockholders	95,248	94,310	113,554
Net income per share attributable to Innoviva stockholders			
Basic	$ 3.07	$ 3.24	$ 2.21
Diluted	$ 2.37	$ 2.87	$ 2.02

Anti-dilutive Securities

The following common stock equivalents were not included in the computation of diluted net income per share because their effect was anti-dilutive:

	Year Ended December 31,		
(In thousands)	**2022**	**2021**	**2020**
Outstanding options and awards granted under equity incentive plan and employee stock purchase plan	648	979	1,193
Outstanding stock warrant	282	—	—
Total	930	979	1,193

3. REVENUE RECOGNITION

Net Revenue from Collaboration Arrangement

On July 13, 2022, Innoviva's wholly owned subsidiary, Innoviva TRC Holdings, LLC ("ITH") entered into an equity purchase agreement ("TRC Equity Purchase Agreement") with Royalty Pharma Investments 2019 ICAV ("Royalty Pharma") to sell our ownership interest in TRC. As a result of the sale of our ownership interest in TRC, which was consummated on July 20, 2022, we are no longer entitled to receive 15% of royalty payments made by GSK stemming from sales of TRELEGY® ELLIPTA®. We retained our royalty rights with respect to RELVAR®/BREO® ELLIPTA® and ANORO® ELLIPTA®.

INNOVIVA, INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

Net revenue recognized under our GSK Agreements was as follows:

	Year Ended December 31,		
(In thousands)	**2022**	**2021**	**2020**
Royalties - RELVAR/BREO	$ 215,034	$ 234,066	$ 221,536
Royalties - ANORO	38,405	44,935	45,992
Royalties - TRELEGY[(1)]	72,029	126,688	73,089
Total royalties	325,468	405,689	340,617
Less: amortization of capitalized fees paid	(13,823)	(13,823)	(13,823)
Royalty revenue	311,645	391,866	326,794
Strategic alliance - MABA program	—	—	10,000
Total net royalty revenue	$ 311,645	$ 391,866	$ 336,794

(1) The year ended December 31, 2022 represents the period from January 1, 2022 to July 20, 2022, the date of the sale of our ownership interest in TRC.

LABA Collaboration

As a result of the launch and approval of RELVAR®/BREO® ELLIPTA® and ANORO® ELLIPTA® in the U.S., Japan and Europe, we paid milestone fees to GSK totaling $220.0 million during the year ended December 31, 2014. The milestone fees paid to GSK were recognized as capitalized fees paid, which are being amortized over their estimated useful lives commencing upon the commercial launch of the product. The amortization is recorded as a reduction to the royalties from GSK.

We are entitled to receive annual royalties from GSK on sales of RELVAR®/BREO® ELLIPTA® as follows: 15% on the first $3.0 billion of annual global net sales and 5% for all annual global net sales above $3.0 billion. Sales of single-agent LABA medicines and combination medicines would be combined for the purposes of this royalty calculation. For other products combined with a LABA from the LABA Collaboration, such as ANORO® ELLIPTA®, royalties are upward tiering and range from 6.5% to 10%.

We are also entitled to 15% of royalty payments made by GSK under its agreements originally entered into with us, and since assigned to TRC in connection with the Spin-Off, including TRELEGY® ELLIPTA®, which royalties are upward tiering and range from 6.5% to 10%.

2004 Strategic Alliance

During the year ended December 31, 2020, we recognized $10.0 million in revenue from a termination fee paid in connection with the termination of the Bifunctional Muscarinic Antagonist-Beta2 Agonist (“MABA”) program under the Strategic Alliance Agreement with GSK.

Net Product Sales

Net product sales we recognized from the date of acquisition of La Jolla, which occurred on August 22, 2022, to December 31, 2022 were $19.7 million, consisting of net sales of GIAPREZA® and XERAVA® for $14.2 million and $5.5 million, respectively. We derived approximately 96% and 4% of our net product sales for the same period from customers located in the U.S. and the rest of the world, respectively.

4. LICENSE AND COLLABORATION ARRANGEMENTS

Out-License Agreements

Zai Lab

Entasis entered into a license and collaboration agreement with Zai Lab (Shanghai) Co., Ltd. ("Zai Lab"), pursuant to which Zai Lab licensed exclusive rights to durlobactam and SUL-DUR, in the Asia-Pacific region ("the Zai Agreement"). Under the terms of the Zai Agreement, Zai Lab will fund most of the registrational clinical trial costs in China for SUL-DUR, with the exception of Phase 3 patient drug supply of licensed products. Zai Lab will conduct development activities and plan and obtain regulatory approval in a specified number of countries in the Asia-Pacific region beyond China after receipt of regulatory approval of a licensed product in China. Zai Lab is also solely responsible for commercializing licensed products in the Asia-Pacific region and will commercialize licensed products for which it has obtained regulatory approval. We are obligated to supply Zai Lab with the licensed products for clinical development and, if the licensed product is approved, for commercial use for a certain period unless Zai Lab notifies otherwise. Zai Lab may take over manufacturing responsibilities for its own commercialization activities within a specified time period following the effective date of the Zai Agreement.

We are eligible to receive up to an aggregate of $91.0 million in research and development support payments and development, regulatory and sales milestone payments related to SUL-DUR, imipenem and other combinations with the licensed products. Zai Lab will pay us a tiered royalty equal to from a high-single digit to low-double digit percentage based on annual net sales of licensed products in the territory, subject to specified reductions for the market entry of competing products, loss of patent coverage of licensed products and for payments owed to third parties for additional rights necessary to commercialize licensed products in the territory. No revenue was recognized under the Zai Agreement from the acquisition date of Entasis. Payments received for research support and reimbursable clinical trial costs are recorded as a reduction to research and development expense during the period in which the qualifying expenses are incurred. Such amounts recorded from the date of acquisition of Entasis to December 31, 2022 are not material.

GARDP

Entasis entered into a collaboration agreement with the Global Antibiotic Research and Development Partnership ("GARDP") for the development, manufacture and commercialization of the product candidate zoliflodacin in certain countries ("the GARDP Collaboration Agreement"). Under the terms of the GARDP Collaboration Agreement, GARDP will use commercially reasonable endeavors to perform and fully fund the Phase 3 registrational trial, including the manufacture and supply of the product candidate containing zoliflodacin, in uncomplicated gonorrhea. We recorded reimbursements from GARDP under this agreement as reduction to research and development expense. Relevant amounts from the date of acquisition of Entasis to December 31, 2022 are not material.

In addition, under the GARDP Collaboration Agreement, GARDP was granted a worldwide, fully paid, exclusive and royalty-free license, with the right to sublicense, to use our zoliflodacin technology in connection with GARDP's development, manufacture and commercialization of zoliflodacin in low-income and specified middle-income countries. We retained commercial rights in all other countries worldwide, including the major markets in North America, Europe and Asia-Pacific. We also retained the right to use and grant licenses to our zoliflodacin technology to perform our obligations under the GARDP Collaboration Agreement and for any purpose other than gonorrhea or community-acquired indications. If we believe that the results of the Phase 3 registrational trial of zoliflodacin would be supportive of an application for marketing approval, we are obligated to use our best efforts to file an application for marketing approval with the FDA within six months of the completion of the trial and to use commercially reasonable endeavors to file an application for marketing approval with the European Medicines Agency ("EMA"). Each party is responsible for using commercially reasonable efforts to obtain marketing authorizations for the product candidate in their respective territories.

PAION AG

Pursuant to the PAION AG ("PAION") License, La Jolla granted PAION an exclusive license to commercialize GIAPREZA® and XERAVA® in the European Economic Area, the United Kingdom and Switzerland (collectively, the "PAION Territory"). We are entitled to receive potential commercial milestone payments of up to $109.5 million and double-digit tiered royalty payments. Royalties payable in a given jurisdiction under the PAION License will be subject to reduction on account of generic competition and after patent expiration in that jurisdiction. Pursuant to the PAION License, PAION will be solely responsible for the future development and commercialization of GIAPREZA® and XERAVA® in the PAION Territory. PAION is required to use commercially reasonable efforts to commercialize GIAPREZA® and XERAVA® in the PAION Territory. We have not recognized any revenue from PAION related to commercial milestones from the date of acquisition of La Jolla to December 31, 2022. Royalty revenue recognized under this agreement from the date of acquisition of La Jolla to December 31, 2022 was not material.

La Jolla also entered into the PAION commercial supply agreement (the "PAION Supply Agreement") whereby La Jolla will supply PAION a minimum quantity of GIAPREZA® and XERAVA® through July 13, 2024. The PAION supply agreement will automatically renew until the earlier of July 13, 2027, or until a new supply agreement is executed. During the initial term of the supply agreement, we will be reimbursed for direct and certain indirect manufacturing costs at cost. Amounts recognized under this agreement from the date of acquisition of La Jolla to December 31, 2022 were not material.

Everest Medicines Limited

Pursuant to the Everest Medicines Limited ("Everest") License, La Jolla granted Everest an exclusive license to develop and commercialize XERAVA® for the treatment of complicated intra-abdominal infections ("cIAI") and other indications in mainland China, Taiwan, Hong Kong, Macau, South Korea, Singapore, the Malaysian Federation, the Kingdom of Thailand, the Republic of Indonesia, the Socialist Republic of Vietnam and the Republic of the Philippines (collectively, the "Everest Territory"). We are eligible to receive an additional $8.0 million regulatory milestone payment and up to an aggregate of $20.0 million in sales milestone payments. We are also entitled to receive tiered royalties from Everest at percentages in the low double digits on sales, if any, in the Everest Territory of products containing eravacycline. Royalties are payable with respect to each jurisdiction in the Everest Territory until the latest to occur of: (i) the last-to-expire of specified patent rights in such jurisdiction in the Everest Territory; (ii) expiration of marketing or regulatory exclusivity in such jurisdiction in the Everest Territory; or (iii) 10 years after the first commercial sale of a product in such jurisdiction in the Everest Territory. We have not recognized any revenue from Everest related to regulatory and sales milestones from the date of acquisition of La Jolla to December 31, 2022. Royalty revenue recognized under this agreement from the date of acquisition of La Jolla to December 31, 2022 was not material.

A new drug application ("NDA") was submitted with the China National Medical Products Administration ("NMPA") for XERAVA® for the treatment of cIAI in patients in China in 2021. XERAVA® was approved in Singapore by the Health Science Authority in 2020.

La Jolla also entered into the Everest commercial supply agreement (the "Everest Supply Agreement") whereby La Jolla will supply Everest a minimum quantity of XERAVA® through December 31, 2023 and will transfer to Everest certain XERAVA®-related manufacturing know-how. We will be reimbursed for direct and certain indirect manufacturing costs at 110% of cost through December 31, 2023. We initially recognized a $2.8 million partial prepayment for XERAVA® as deferred revenue, of which, $0.8 million was recognized as revenue for the year ended December 31, 2022.

In-License Agreements

George Washington University

Pursuant to the George Washington University ("GW") License, GW exclusively licensed to La Jolla certain intellectual property rights relating to GIAPREZA®, including the exclusive rights to certain issued patents and patent applications covering GIAPREZA®. Under the GW License, we are obligated to use commercially reasonable efforts to develop, commercialize, market and sell GIAPREZA®. We are obligated to pay a 6% royalty on net sales of GIAPREZA® and 15% on payments received from sublicensees. The obligation to pay royalties under this agreement extends through the last-to-expire patent covering GIAPREZA®. From the date of acquisition of La Jolla to December 31, 2022, the amounts recognized under this agreement were not material.

Harvard University

Pursuant to the Harvard University ("Harvard") License, Harvard exclusively licensed to La Jolla certain intellectual property rights relating to tetracycline-based products, including XERAVA®, including the exclusive rights to certain issued patents and patent applications covering such products. Under the Harvard License, we are obligated to use commercially reasonable efforts to develop, commercialize, market and sell tetracycline-based products, including XERAVA®. For each product covered by the Harvard License, we are obligated to make certain payments for the following: (i) up to approximately $15.1 million upon the achievement of certain clinical development and regulatory milestones; (ii) a 5% royalty on direct U.S. net sales of XERAVA®; (iii) a single-digit tiered royalty on direct ex-U.S. net sales of XERAVA®, starting at a minimum royalty rate of 4.5%, with step-ups to a maximum royalty of 7.5% based on the achievement of annual net product sales thresholds; and (iv) 20% on payments received from sublicensees. The obligation to pay royalties under this agreement extends through the last-to-expire patent covering tetracycline-based products, including XERAVA®. From the date of acquisition of La Jolla to December 31, 2022, amounts recognized under this agreement were not material.

Paratek Pharmaceuticals, Inc.

Pursuant to the Paratek Pharmaceuticals, Inc. ("Paratek") License, Paratek non-exclusively licensed to La Jolla certain intellectual property rights relating to XERAVA®, including non-exclusive rights to certain issued patents and patent applications covering XERAVA®. We are obligated to pay Paratek a 2.25% royalty based on direct U.S. net sales of XERAVA®. Our obligation to pay royalties with respect to the licensed product is retroactive to the date of the first commercial sale of XERAVA® and shall continue until there are no longer any valid claims of the Paratek patents, which will expire in October 2023. From the date of acquisition of La Jolla to December 31, 2022, amounts recognized under this agreement were not material.

5. CONSOLIDATED ENTITIES AND ACQUISITIONS

Consolidated Entities

Theravance Respiratory Company, LLC

Up until July 20, 2022, we consolidated TRC under the VIE model as we determined that TRC was a VIE and we were the primary beneficiary of the entity because we had the power to direct the economically significant activities of TRC and the obligation to absorb losses of, or the right to receive benefits from, TRC. We held 15% ownership interest of TRC. The primary source of revenue for TRC is the royalties generated from the net sales of TRELEGY® ELLIPTA® by GSK.

As discussed in Note 3, "Revenue Recognition", on July 13, 2022, ITH entered into the TRC Equity Purchase Agreement to sell our ownership interest in TRC. Upon the closing of the transaction on July 20, 2022, we received $277.5 million in cash from Royalty Pharma. We are also entitled to receive up to $50.0 million in contingent sales-based milestone payments in the future. In connection with the closing of the transaction, we also received our portion of TRC's remaining cash balance of $4.4 million from Royalty Pharma rather than through a cash distribution from TRC.

Prior to the closing of the transaction and as part of the agreement, TRC distributed its ownership interests and investments in InCarda Therapeutics, Inc., ImaginAb, Inc., Gate Neurosciences, Inc. and Nanolive SA, which had a total carrying value of $39.4 million, to ITH. We accounted for the transaction similar to an upstream sale between a parent and a VIE under ASC 810-10. As such,

ITH recorded the transferred investments at their respective carrying values and no gain or loss was recognized in the consolidated statement of income.

The summarized financial information for TRC as of December 31, 2021 and for the relevant periods through the sale date in 2022 are presented as follows:

Balance sheet

(In thousands)	December 31, 2021
Assets	
Cash and cash equivalents	$ 50,713
Receivables from collaborative arrangements	42,492
Prepaid expenses and other current assets	71
Equity and long-term investments	37,695
Total assets	$ 130,971
Liabilities and LLC Members' Equity	
Current liabilities	$ 252
LLC members' equity	130,719
Total liabilities and LLC members' equity	$ 130,971

Income statements

	Year Ended December 31,		
(In thousands)	2022 [1]	2021	2020
Royalty revenue	$ 72,029	$ 126,688	$ 73,089
Revenue from collaborative arrangements	—	—	10,000
Total net revenue	72,029	126,688	83,089
Operating expenses	332	3,956	2,612
Income from operations	71,697	122,732	80,477
Other income, net	10	—	38
Realized loss	(39,386)	—	—
Income tax expense, net	1	—	—
Changes in fair values of other equity and long-term investments	(8,884)	(1,541)	1,147
Net income	$ 23,438	$ 121,191	$ 81,662

[1] The year ended December 31, 2022 represents the period from January 1, 2022 to July 20, 2022, the date of the sale of our ownership interest in TRC.

ISP Fund LP

In December 2020, Innoviva Strategic Partners LLC, our wholly owned subsidiary ("Strategic Partners"), contributed $300.0 million to ISP Fund LP (the "Partnership") for investing in "long" positions in the healthcare, pharmaceutical and biotechnology sectors and became a limited partner. The general partner of the Partnership ("General Partner") is an affiliate of Sarissa Capital.

The Partnership Agreement provides for Sarissa Capital to receive management fees from the Partnership, payable quarterly in advance, measured based on the Net Asset Value of Strategic Partners' capital account in the Partnership. In addition, the General Partner is entitled to an annual performance fee based on the Net Profits of the Partnership during the annual measurement period.

The Partnership Agreement includes a lock-up period of thirty-six months after which Strategic Partners is entitled to make withdrawals from the Partnership as of such lock-up expiration date and each anniversary thereafter, subject to certain limitations.

In May 2021, Strategic Partners received a distribution of $110.0 million from the Partnership to provide funding to Innoviva for a strategic repurchase of the Company's shares held by GSK. On March 30, 2022, Strategic Partners made an additional capital contribution of $110.0 million to the Partnership pursuant to the letter agreement entered into between Strategic Partners, the Partnership and Sarissa Capital Fund GP LP on May 20, 2021. The capital contribution is subject to a 36-month lock up period from the contribution date

We consolidate ISP Fund LP under the VIE model as we have determined that ISP Fund LP is a VIE and we are the primary beneficiary of the entity via our related party relationships with Sarissa Capital entities.

As of December 31, 2022, we continued to hold 100% of the economic interest of Partnership. As of December 31, 2022 and 2021, total assets of the Partnership were $320.6 million and $195.8 million, respectively, of which the majority was attributable to equity, debt and long-term investments. As of December 31, 2022 and 2021, total liabilities of the Partnership were $1.6 million and $0.2 million, respectively. The Partnership's assets can only be used to settle its own obligations. During the year ended December 31, 2022, the Partnership incurred $5.2 million in net investment-related expenses, generated $2.0 million interest income, recorded $6.8 million in net realized gains and $9.9 million in net unrealized losses as changes in fair values of other equity and long-term investments, net, on the consolidated statements of income. During the year ended December 31, 2021, the Partnership incurred $3.6 million in net investment-related expense, generated $1.8 million interest and dividend income, and recorded net $10.5 million realized gains and net $2.4 million unrealized losses as changes in fair values of other equity and long-term investments, net, on the consolidated statements of income. We account for the long-term investments held by ISP Fund LP as equity investments measured at fair value and an investment in convertible notes as trading security.

Acquisitions

Entasis Therapeutics Holdings Inc.

We started investing in Entasis in 2020 as part of our capital allocation strategy of deploying cash generated from royalty income and investing in different life sciences companies. Entasis is an advanced, late clinical-stage biopharmaceutical company focused on the discovery and development of novel antibacterial products. During the second quarter of 2020, we purchased 14,000,000 shares of common stock as well as warrants to purchase 14,000,000 additional shares of common stock of Entasis for approximately $35.0 million in cash. During the third quarter of 2020, we purchased 4,672,897 shares of Entasis common stock as well as warrants to purchase 4,672,897 additional shares of its common stock for approximately $12.5 million in cash. Effective in June 2020, after certain conditions were met with respect to the sales of Entasis equity shares, Innoviva had the right to designate two members to Entasis' board of directors. During the second quarter of 2021, Innoviva's wholly owned subsidiary, Innoviva Strategic Opportunities, LLC ("ISO") entered into a securities purchase agreement with Entasis to acquire 10,000,000 shares of Entasis common stock and warrants to purchase 10,000,000 additional shares of Entasis common stock for approximately $20.0 million.

The fair value of Entasis' common stock was measured based on its closing market price at each balance sheet date. The warrants had an exercise price of $2.50 per share and $2.675 per share for those warrants acquired in the second and third quarter of 2020, respectively. The warrants acquired in the second quarter of 2021 had an exercise price of $2.00 per share. All of the warrants were exercisable immediately within five years from the issuance date of the warrants and included a cashless exercise option. We used the Black-Scholes-Merton pricing model to estimate the fair value of these warrants.

On February 17, 2022, ISO entered into a securities purchase agreement with Entasis pursuant to which ISO purchased a convertible promissory note for a total purchase price of $15.0 million. The note bore an annual interest rate of 0.59% and was due to mature and become payable on August 18, 2022 unless it was converted at a conversion price of $1.48 before the maturity date. With this financing, we determined that we had both (i) the power to direct the economically significant activities of Entasis and (ii) the obligation to absorb the losses, or the right to receive the benefits, that could potentially be significant to Entasis and therefore, we were the primary beneficiary of Entasis. Accordingly, we consolidated Entasis' financial position and results of operations effective on February 17, 2022. Our equity ownership interest remained at 59.9% as of February 17, 2022, and the fair values of our holdings of Entasis common stock and warrants were remeasured and estimated at $64.5 million and $31.4 million, respectively.

The remeasurement resulted in a $7.8 million loss in the first quarter of 2022 which was included in changes in fair values of equity method investments, net, on the consolidated statements of income for the year ended December 31, 2022.

We completed our acquisition of Entasis' remaining noncontrolling interest on July 11, 2022. We remeasured our holdings in Entasis as of that date and recognized a $1.4 million loss, which was included in changes in fair values of equity method investments, net, on the consolidated statement of income for the year ended December 31, 2022. No payments were made toward the convertible promissory note through the date of acquisition of Entasis. In connection with the acquisition, all of the Entasis warrants were replaced with Innoviva warrants (the "Replacement Warrants") of equivalent value and bearing the same terms. The Replacement Warrants are classified as equity.

We recognized the difference between the acquisition price and the carrying value of the acquired noncontrolling interest on July 11, 2022 in our additional paid-in capital.

The fair values assigned to assets acquired and liabilities assumed as of February 17, 2022 were based on management's best estimates and assumptions. After the acquisition in July 2022, we adjusted the preliminary estimates of fair value of assets acquired and liabilities assumed based on new and additional information related to product sales forecast provided by Entasis and deferred tax liabilities.

During the year ended December 31, 2022, we recorded measurement period adjustments of $4.7 million decrease in goodwill, primarily related to a decrease in estimated purchase price of $1.4 million, an increase in noncontrolling interests of $1.7 million, and an increase in intangible assets of $2.5 million. The cumulative impact of the measurement period adjustments included in the consolidated net income for the year ended December 31, 2022 was not material.

The Company has completed a preliminary valuation and expects to finalize it as soon as practical, but no later than one year from the acquisition date. The purchase accounting for this transaction is not yet finalized.

The following table represents the adjusted fair values of the assets acquired and liabilities assumed by us in the transaction:

(In thousands)	February 17, 2022
Cash and cash equivalents	$ 23,070
Prepaid expenses	5,554
Other current assets	1,959
Property and equipment, net	185
Right-of-use assets	959
Goodwill	10,260
Intangible assets	107,500
Other assets	302
Total assets acquired	$ 149,789
Accounts payable	$ 1,583
Accrued personnel-related expenses	1,058
Other accrued liabilities	5,096
Deferred tax liabilities	7,336
Total liabilities assumed	$ 15,073
Total assets acquired, net	$ 134,716

The goodwill arising from the acquisition of Entasis is primarily attributable to Entasis' assembled workforce and the value associated with growing our business more efficiently. The goodwill from this acquisition is not expected to be deductible for tax purposes.

Refer to Note 8, "Goodwill and Intangible Assets", for more discussion on the intangible assets recognized as part of this acquisition.

Our consolidated net income for the year ended December 31, 2022 included the net loss attributable to noncontrolling interest since the consolidation date until the date of acquisition of $13.6 million.

INNOVIVA, INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

La Jolla Pharmaceutical Company

On August 22, 2022, ISO acquired La Jolla for a total consideration of $206.6 million. ISO acquired La Jolla at a price of $6.23 per share. La Jolla is dedicated to the commercialization of innovative therapies that improve outcomes in patients suffering from life-threatening diseases. La Jolla brings to Innoviva an established product portfolio, including GIAPREZA® (angiotensin II), approved to increase blood pressure in adults with septic or other distributive shock and XERAVA® (eravacycline) for the treatment of cIAIs.

The fair values assigned to assets acquired and liabilities assumed are based on management's best estimates and assumptions as of August 22, 2022.

During the year ended December 31, 2022, we recorded measurement period adjustments of $3.7 million increase in goodwill, primarily related to a decrease in inventory and intangible assets of $7.7 million and $1.5 million, respectively, and an increase in deferred tax liabilities of $2.6 million, partially offset by a decrease in other long-term liabilities of $8.3 million. The cumulative impact of the measurement period adjustments included in the consolidated net income for the year ended December 31, 2022 was not material.

We have completed a preliminary valuation and expect to finalize it as soon as practicable, but no later than one year from the acquisition date. The purchase accounting for this transaction is not yet finalized.

We incurred approximately $5.3 million in acquisition-related costs in connection with this acquisition and such amount is included in selling, general and administrative expenses for the year ended December 31, 2022.

The following table summarizes the adjusted allocation of the fair values assigned to the assets acquired and liabilities assumed as of the date of the acquisition:

(In thousands)	August 22, 2022
Cash and cash equivalents	$ 47,415
Short-term marketable securities	471
Accounts receivable	5,876
Inventory	66,200
Prepaid expenses	1,261
Other current assets	907
Property and equipment, net	13
Right-of-use assets	226
Goodwill	16,453
Intangible assets	151,000
Other assets	710
Total assets acquired	$ 290,532
Accounts payable	$ 1,237
Deferred revenue	2,849
Other accrued liabilities	11,362
Other long-term liabilities	65,944
Deferred tax liabilities	2,581
Total liabilities assumed	$ 83,973
Total assets acquired, net	$ 206,559

The goodwill arising from the acquisition of La Jolla is primarily attributable to La Jolla's assembled workforce and the value associated with leveraging the workforce to develop and commercialize new drug products in the future and growing our business more efficiently. The goodwill from this acquisition is not expected to be deductible for tax purposes.

Refer to Note 8, "Goodwill and Intangible Assets", for more discussion on the intangible assets recognized as part of this acquisition.

Pro Forma Financial Information

The following table presents certain unaudited pro-forma financial information for the years ended December 31, 2022 and 2021 as if the consolidation of Entasis and La Jolla occurred on January 1, 2021. The unaudited pro forma financial information is presented for informational purposes only, and is not indicative of the results of operations that would have been achieved if the acquisitions had taken place on January 1, 2021, or of results that may occur in the future. The unaudited pro forma financial information combines the historical results of the Entasis and La Jolla with the Company's consolidated historical results and includes certain adjustments including, but not limited to, fair value adjustments to equity investments in Entasis' common stock and warrants, fair value adjustments to inventory, amortization of intangible assets, and interest expense on deferred royalty obligations and acquisition-related costs.

	Year Ended December 31,	
(In thousands)	2022	2021
Revenue	$ 357,880	$ 435,398
Net income	$ 204,987	$ 281,719
Net income attributable to Innoviva stockholders	$ 214,390	$ 197,535

6. EQUITY AND LONG-TERM INVESTMENTS AND FAIR VALUE MEASUREMENTS

Equity Method Investment in Armata

During the first quarter of 2020, Innoviva acquired 8,710,800 shares of common stock as well as warrants to purchase 8,710,800 additional shares of common stock of Armata Pharmaceuticals, Inc. ("Armata") for approximately $25.0 million in cash. Armata is a clinical stage biotechnology company focused on precisely targeted bacteriophage therapeutics for antibiotic-resistant infections.

During the first quarter of 2021, ISO entered into a securities purchase agreement with Armata to acquire 6,153,847 shares of Armata common stock and warrants to purchase 6,153,847 additional shares of Armata common stock for approximately $20.0 million. Armata also entered into a voting agreement with the Company and ISO, pursuant to which the Company and ISO agreed not to vote or take any action by written consent with respect to any common shares held by the Company and ISO that represent, in the aggregate, more than 49.5% of the total number of shares of Armata's common stock for voting on the matters related to election or removal of Armata's board members. The voting agreement will expire the earlier of the second anniversary of the agreement effective date and approval by the FDA of any of Armata's product candidates for marketing and commercial distribution. During the fourth quarter of 2021, ISO also purchased an additional 1,212,122 shares of Armata common stock for approximately $4.0 million.

On February 9, 2022, ISO entered into a securities purchase agreement with Armata to acquire 9,000,000 shares of Armata common stock and warrants to purchase 4,500,000 additional shares of common stock with an exercise price of $5.00 per share for $45.0 million. The investment closed in two tranches on February 9, 2022 and March 31, 2022. The investment is intended to aid Armata in advancing its clinical pipeline and strengthening its bacteriophage platform. On February 9, 2022, Armata also entered a second amended and restated voting agreement with the Company and ISO, pursuant to which the Company and ISO agreed not to vote or take any action by written consent with respect to any common shares held by the Company and ISO that represent, in the aggregate, more than 49.5% of the total number of shares of Armata's common stock for voting on the matters related to election or removal of Armata's board members or amend the bylaws of Armata to reduce the maximum number of directors or set the number of directors who may serve on the board of Armata. The voting agreement will expire the earlier of the second anniversary of the agreement effective date and approval by the FDA of any of Armata's product candidates for marketing and commercial distribution. In addition, as of February 9, 2022, Armata entered into an amended and restated investor rights agreement with the Company and ISO, pursuant to which for as long as the Company and ISO hold at least 12.5% of the outstanding shares of Armata's common stock on a fully-diluted, the Company and ISO shall have the right to designate two directors to Armata's board of directors, and for so long as the Company and ISO hold at least 8%, but less than 12.5%, of the outstanding shares of Armata's common stock on a fully-diluted basis, the Company and ISO shall have the right to designate one director to Armata's board of directors, subject to certain conditions and qualifications set forth in the amended and restated investor rights agreement. As of December 31, 2022, three of the eight members of Armata's board of directors are also members of the board of directors of Innoviva. As of December 31, 2022 and 2021, we owned approximately 69.4% and 59.3%, respectively, of Armata's common stock.

The investments in Armata provide Innoviva and ISO the ability to have significant influence, but not control over Armata's operations. Armata's business and affairs are managed under the direction of its board of directors, which Innoviva and ISO do not control. Based on our evaluation, we determined that Armata is a VIE, but Innoviva and ISO are not the primary beneficiary of the VIE. We have not provided financial or other support that we were not previously contractually required to provide during the periods presented. Our maximum exposure to loss is equal to the amount we invested in the entity.

We account for both Armata's common stock and warrants under the equity method using the fair value option. The fair value of Armata's common stock is measured based on its closing market price. The warrants purchased in 2020, 2021 and 2022 have an exercise price of $2.87, $3.25 and $5.00 per share, respectively. All warrants are exercisable immediately within five years from the issuance date of the warrants and include a cashless exercise option. We use the Black-Scholes-Merton pricing model to estimate the fair value of these warrants with the following input assumptions: Armata's closing market price on the valuation date, the risk-free interest rate computed based on the U.S. Treasury yield, the remaining contractual term as the expected term, and the expected stock price volatility calculated based on the historical volatility of the common stock of Armata and its peer companies.

As of December 31, 2022, the fair values of our holdings of Armata common stock and warrants were estimated at $31.1 million and $8.1 million, respectively. As of December 31, 2021, the fair values of our holdings of Armata common stock and warrants were estimated at $88.1 million and $58.6 million, respectively. The total fair value of both financial instruments in the amount of $39.2 million and $146.7 million was recorded as equity and long-term investments on the consolidated balance sheets as of December 31, 2022 and 2021, respectively. We recorded $152.5 million unrealized losses and $78.7 million unrealized gains as changes in fair values of equity method investments, net, on the consolidated statements of income for the years ended December 31, 2022 and 2021, respectively.

The summarized financial information, including the portion we do not own, is presented for Armata on a one quarter lag regardless of the date of our investments as follows:

Balance Sheet Information

	September 30,	
(In thousands)	**2022**	**2021**
Current assets	$ 33,245	$ 14,178
Noncurrent assets	$ 59,636	$ 28,493
Current liabilities	$ 7,004	$ 5,254
Noncurrent liabilities	$ 40,300	$ 13,662

Income Statement Information

	Twelve Months Ended September 30,		Nine Months Ended September 30,
(In thousands)	**2022**	**2021**	**2020**
Revenue	$ 5,446	$ 3,989	$ 319
Loss from operations	$ (32,666)	$ (24,227)	$ (15,134)
Net loss	$ (32,650)	$ (23,732)	$ (15,557)

Equity Method Investment in Entasis

Prior to the consolidation of Entasis' financial position and results of operations in February 2022, we accounted for Entasis as an equity method investment. Refer to Note 5, "Consolidated Entities and Acquisitions", for more information.

The summarized financial information, including the portion we did not own, is presented for Entasis on a one quarter lag regardless of the date of our investments as follows:

Balance Sheet Information

(In thousands)	September 30, 2021
Current assets	$ 49,746
Noncurrent assets	$ 1,020
Current liabilities	$ 9,348
Noncurrent liabilities	$ 183

Income Statement Information

(In thousands)	Twelve Months Ended September 30, 2021	Six Months Ended September 30, 2020
Loss from operations	$ (52,323)	$ (26,080)
Net loss	$ (125,413)	$ (24,529)

Equity Investment in InCarda

During the third quarter of 2020, TRC purchased 20,469,432 shares of Series C preferred stock and a warrant to purchase 5,117,358 additional shares of Series C preferred stock of InCarda Therapeutics, Inc. ("InCarda") (the "InCarda 2020 Warrant") for $15.8 million, which included $0.8 million of transaction costs. InCarda is a privately held biopharmaceutical company focused on developing inhaled therapies for cardiovascular diseases. The investment is intended to fund the ongoing clinical development of InRhythmTM (flecainide for inhalation), InCarda's lead program, for the treatment of a recent-onset episode of paroxysmal atrial fibrillation. On July 20, 2022, under the terms of the TRC Equity Purchase Agreement, TRC transferred to ITH all of TRC's ownership interests and investments in InCarda. ITH has the right to designate one member to InCarda's board of directors. As of December 31, 2022, one of InCarda's eight board members was designated by ITH. The InCarda 2020 Warrant is exercisable immediately with an exercise price of $0.7328 per share. In September 2021, TRC and InCarda entered into an amendment to extend the expiration date of the InCarda 2020 Warrant from October 6, 2021 to March 31, 2022. On March 9, 2022, TRC and InCarda entered into an amendment to further extend the expiration date of the InCarda 2020 Warrant from March 31, 2022 to March 31, 2023. The InCarda 2020 Warrant is recorded at fair value and subject to remeasurement at each balance sheet date.

On March 9, 2022, TRC entered into a Note and Warrant Purchase Agreement (the "InCarda Agreement") with InCarda to acquire a convertible promissory note (the "InCarda Convertible Note") and warrants (the "InCarda 2022 Warrant") for $0.7 million. The InCarda Convertible Note bears an annual interest rate of 6% and will convert into Series D preferred stock upon a qualified financing, non-qualified financing, or maturity conversion. A qualified financing is defined as the first issuance or series of related issuances by InCarda of its equity securities following March 9, 2022 from which InCarda receives immediately available gross proceeds of at least $10.0 million (excluding the aggregate amount of any notes converted into equity securities pursuant to the conversion of notes or any other debt securities converted into equity securities) (the "Qualified Financing Amount"). A non-qualified financing is defined as the first issuance or series of related issuances by InCarda of its equity securities following March 9, 2022 from which InCarda receives immediately available gross proceeds of less than the Qualified Financing Amount. The InCarda 2022 Warrant entitles TRC to purchase a number of shares of equity securities equal to 100% of the principal amount of the InCarda Convertible Note divided by the number of shares issued in InCarda's next equity financing, which is defined as the earliest to occur of specific financing events, including capital raises through public offerings. The InCarda 2022 Warrant expires on March 9, 2027. The InCarda Convertible Note and InCarda 2022 Warrant are measured at fair value.

On June 15, 2022, the principal amount and the accrued interest of the InCarda Convertible Note were converted into equity securities. In addition, TRC participated in InCarda's Series D preferred stock financing by investing $2.3 million. In connection with the new round of financing, InCarda recapitalized its equity structure resulting in TRC owning 4,093,886 shares of InCarda's common

stock, 37,350 shares of its Series A-1 preferred stock, 20,469,432 shares of its Series C preferred stock, 8,771,780 shares of its Series D-1 preferred stock, 3,369,802 shares of its Series D-2 preferred stock, a warrant to purchase 5,117,358 shares of its Series C preferred stock at $0.73 per share and a warrant to purchase 2,490,033 shares of its Series D-1 preferred stock at $0.20 per share.

As of December 31, 2022 and 2021, we held 9.0% and 13.0% of InCarda equity ownership, respectively. Our investment in InCarda does not provide us with the ability to control or have significant influence over InCarda's operations. Based on our evaluation, we determined that InCarda is a VIE, but we are not the primary beneficiary of the VIE. We have not provided financial or other support that we were not previously contractually required to provide during the periods presented. Our maximum exposure to loss is equal to the amount we invested in the entity.

We account for our investments in InCarda under the measurement alternative. Under the measurement alternative, the equity investment is initially recorded at its allocated cost, but the carrying value may be adjusted through earnings upon an impairment or when there is an observable price change involving the same or a similar investment with the same issuer. Due to InCarda's equity recapitalization in the second quarter of 2022, TRC reassessed the value of its investments in InCarda using the Option Pricing Model Backsolve valuation methodology. Key assumptions used in the valuation model include an expected holding period of two years, a risk free interest rate of 3.2%, a dividend yield of 0.0% and an estimated volatility of 122.0%. The estimated volatility is calculated based on the historical volatility of a selected peer group of public companies comparable to InCarda. We recognized an impairment charge of $9.0 million as a result of the valuation. There was no impairment or other change to the value of our investments in InCarda as of December 31, 2021.

As of December 31, 2022, we recorded $6.8 million in fair value of InCarda's Series C preferred stock and $0.6 million in fair value of Series C warrants and Series D warrants (the "InCarda Preferred Stock Warrants"). As of December 31, 2022, we recognized $3.2 million for InCarda's Series D-1 preferred stock, Series D-2 preferred stock, and common stock using the measurement alternative. As of December 31, 2021, we recorded $0.4 million in fair value of the InCarda 2020 Warrant. As of December 31, 2021, we recognized $15.8 million for the investment in InCarda's Series C preferred stock using the measurement alternative. We recorded $8.7 million and $0.7 million unrealized loss as changes in fair values of other equity and long-term investments, net, on the consolidated statements of income for the years ended December 31, 2022 and 2021, respectively.

Equity Investment in ImaginAb

On March 18, 2021, TRC entered into a securities purchase agreement with ImaginAb, Inc. ("ImaginAb") to purchase 4,051,724 shares of ImaginAb Series C preferred stock for $4.7 million. On the same day, TRC also entered into a securities purchase agreement with one of ImaginAb's common stockholders to purchase 4,097,157 shares of ImaginAb common stock for $1.3 million. ImaginAb is a privately held biotechnology company focused on clinically managing cancer and autoimmune diseases via molecular imaging. $0.4 million was incurred for investment due diligence costs and execution and recorded as part of the equity and long-term investment on the consolidated balance sheets.

On July 20, 2022, under the terms of the TRC Equity Purchase Agreement, TRC transferred to ITH all of TRC's ownership interests and investments in ImaginAb. As of December 31, 2022, one of ImaginAb's six board members is designated by ITH, and ITH held 12.7% of ImaginAb's equity ownership. As of December 31, 2021, TRC held 14.5% of ImaginAb equity ownership.

Our investment in ImaginAb does not provide us with the ability to control or have significant influence over ImaginAb's operations. Based on our evaluation, we determined that ImaginAb is a VIE, but we are not the primary beneficiary of the VIE. We have not provided financial or other support that we were not previously contractually required to provide during the periods presented. Our maximum exposure to loss is equal to the amount we invested in the entity.

Because ImaginAb's equity securities are not publicly traded and do not have a readily determinable fair value, we account for our investment in ImaginAb's Series C preferred stock and common stock using the measurement alternative. Under the measurement alternative, the equity investment is initially recorded at its allocated cost, but the carrying value may be adjusted through earnings upon an impairment or when there is an observable price change involving the same or a similar investment with the same issuer. As of December 31, 2022 and 2021, $6.4 million was recorded as equity and long-term investments on the consolidated balance sheets and there was no change to the fair value of our investment in ImaginAb.

Convertible Promissory Note in Gate Neurosciences

On November 24, 2021, TRC entered into a Convertible Promissory Note Purchase Agreement with Gate Neurosciences, Inc. ("Gate") to acquire a convertible promissory note (the "Convertible Note") with a principal amount of $15.0 million. Gate is a privately held biopharmaceutical company focused on developing the next generation of targeted nervous system therapies, leveraging precision medicine approaches to develop breakthrough drugs for psychiatric and neurologic diseases. The investment is intended to fund its ongoing development and research. The Convertible Note bears an annual interest rate of 8% and will convert into common stock shares upon a qualified event or into shares of shadow preferred stock ("Shadow Preferred") upon a qualified financing. A qualifying event can be a qualified initial price offering, a qualified merger, or a merger with a special-purpose acquisition company ("SPAC"). Shadow Preferred means preferred stock having identical rights, preferences and restrictions as the preferred stock that would be issued in a qualified financing.

The number of common stock shares to be issued in a qualified event shall be equal to the amount due on the conversion date divided by the lesser of a capped conversion price (the "Capped Conversion Price") and the qualified event price (the "Qualified Event Price"). The Capped Conversion Price is calculated as $50.0 million divided by the number of common stock outstanding at such time on a fully diluted basis. The Qualified Event Price is the price per share determined by the qualified event. A qualified financing is a sale or series of sales of preferred stock where (i) at least 50 percent of counterparties are not existing shareholders, (ii) net proceeds to Gate are at least $35.0 million, and (iii) the stated or implied equity valuation of Gate is at least $80.0 million.

On July 20, 2022, under the terms of the TRC Equity Purchase Agreement, TRC transferred to ITH its debt investment in Gate. We have accounted for the Gate Convertible Note as a trading security, measured at fair value using a Monte Carlo simulation model with the probability of certain qualified events and the assumptions of equity value of Gate, risk-free rate, expected stock price, volatility of its peer companies, and the time until a financing is raised. As of December 31, 2022 and 2021, the fair value of the Gate Convertible Note was estimated at $15.7 million and $15.1 million, respectively, and recorded as equity and long-term investments on the consolidated balance sheets. We recorded $0.6 million of unrealized gain and $0.8 million of unrealized loss as changes in fair values of other equity and long-term investments, net, on the consolidated statements of income for the years ended December 31, 2022 and 2021, respectively.

Equity Investment in Nanolive

On February 18, 2022, TRC entered into an investment and shareholders agreement with Nanolive SA ("Nanolive") to purchase 18,750,000 shares of Nanolive Series C preferred stock for $9.8 million (equivalent to 9.0 million CHF). Nanolive SA is a Swiss privately held life sciences company focused on developing breakthrough imaging solutions that accelerate research in growth industries such as drug discovery and cell therapy. $0.7 million was incurred for investment due diligence costs and execution and recorded as part of the equity and long-term investment on the consolidated balance sheets. On July 20, 2022, under the terms of the TRC Equity Purchase Agreement, TRC transferred to ITH all of TRC's ownership interests and investments in Nanolive. ITH has the right to designate one member to Nanolive's board. ITH also has the right to designate another member, who will be mutually acceptable to ITH and another majority common stockholder, to Nanolive's board. As of December 31, 2022, one of Innoviva designees is serving on Nanolive's seven-member board. As of December 31, 2022, we held 15.5% of Nanolive equity ownership.

Our investment in Nanolive does not provide us with the ability to control or have significant influence over Nanolive's operations. Based on our evaluation, we determined that Nanolive is a VIE, but we are not the primary beneficiary of the VIE. We have not provided financial or other support that we were not previously contractually required to provide during the periods presented. Our maximum exposure to loss is equal to the amount we invested in the entity.

Because Nanolive's equity securities are not publicly traded and do not have a readily determinable fair value, we account for our investment in Nanolive's Series C preferred stock using the measurement alternative. As of December 31, 2022, $10.6 million was recorded as equity and long-term investments on the consolidated balance sheets and there was no change to the fair value of our investment.

Available-for-Sale Securities

The estimated fair value of available-for-sale securities is based on quoted market prices for these or similar investments that were based on prices obtained from a commercial pricing service. Available-for-sale securities are summarized below:

	December 31, 2022			
(In thousands)	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
Money market funds[1]	$ 263,469	$ —	$ —	$ 263,469
Total	$ 263,469	$ —	$ —	$ 263,469

(1) Money market funds are included in cash and cash equivalents on the consolidated balance sheets.

	December 31, 2021			
(In thousands)	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
Money market funds[1]	$ 145,132	$ —	$ —	$ 145,132
Total	$ 145,132	$ —	$ —	$ 145,132

(1) Money market funds are included in cash and cash equivalents on the consolidated balance sheets.

As of December 31, 2022, all investments were money market funds, and there was no credit loss recognized.

INNOVIVA, INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

Fair Value Measurements

Our available-for-sale securities, equity and long-term investments are measured at fair value on a recurring basis and our debt is carried at amortized cost basis. The estimated fair values were as follows:

	Estimated Fair Value Measurements as of December 31, 2022 Using:			
Types of Instruments (In thousands)	**Quoted Price in Active Markets for Identical Assets Level 1**	**Significant Other Observable Inputs Level 2**	**Significant Unobservable Inputs Level 3**	**Total**
Assets				
Money market funds	$ 263,469	$ —	$ —	$ 263,469
Investments held by ISP Fund LP [1]	265,982	—	54,578	320,560
Equity investment - Armata Common Stock	31,095	—	—	31,095
Equity investment - Armata Warrants	—	8,059	—	8,059
Equity investment - InCarda Warrants	—	—	605	605
Convertible debt investment - Gate Note	—	—	15,700	15,700
Total assets measured at estimated fair value	$ 560,546	$ 8,059	$ 70,883	$ 639,488
Liabilities				
Debt				
2023 Notes	$ —	$ 96,089	$ —	$ 96,089
2025 Notes	—	197,807	—	197,807
2028 Notes	—	211,768	—	211,768
Total fair value of debt	$ —	$ 505,664	$ —	$ 505,664
Contingent value rights	—	—	595	595
Total liabilities at estimated fair value	$ —	$ 505,664	$ 595	$ 506,259

[1] The investments held by ISP Fund LP, consisted of $295.4 million in equity investments, which included private placement positions and convertible notes of $54.6 million, and $25.1 million in money market funds. Our total capital contribution of $300.0 million is subject to a 36-month lock-up period from the date of such capital contributions.

	Estimated Fair Value Measurements as of December 31, 2021 Using:			
Types of Instruments (In thousands)	**Quoted Price in Active Markets for Identical Assets Level 1**	**Significant Other Observable Inputs Level 2**	**Significant Unobservable Inputs Level 3**	**Total**
Assets				
Money market funds	$ 145,132	$ —	$ —	$ 145,132
Investments held by ISP Fund LP [1]	193,677	—	2,068	195,745
Equity investment - Armata Common Stock	88,101	—	—	88,101
Equity investment - Armata Warrants	—	58,595	—	58,595
Equity investment - Entasis Common Stock	62,794	—	—	62,794
Equity investment - Entasis Warrants	—	40,914	—	40,914
Equity investment - InCarda Warrants	—	—	411	411
Convertible debt investment - Gate Note	—	—	15,100	15,100
Total assets measured at estimated fair value	$ 489,704	$ 99,509	$ 17,579	$ 606,792
Debt				
2023 Notes	$ —	$ 261,769	$ —	$ 261,769
2025 Notes	—	234,498	—	234,498
Total fair value of debt	$ —	$ 496,267	$ —	$ 496,267

[1] The investments held by ISP Fund LP, consisted of $192.2 million equity investments and $3.5 million money market funds, are subject to a 36-month lock-up period from our initial contribution date, December 11, 2020.

The fair values of our equity investments in Armata's and Entasis's common stock and public traded investments held by ISP Fund LP are based on the quoted prices in active markets and are classified as Level 1 financial instruments. The fair values of the warrants of Armata and Entasis classified within Level 2 are based upon observable inputs that may include benchmark yields, reported trades, broker/dealer quotes, issuer spreads, two-sided markets, benchmark securities, bids, offers and reference data including market research publications.

InCarda's equity securities, Gate's convertible note, private placement positions and convertible notes held by ISP Fund LP, and contingent value rights are classified as Level 3 financial instruments as these securities are not publicly traded and the assumptions used in the valuation model for valuing these securities are based on significant unobservable and observable inputs including those of publicly traded peer companies.

The fair values of our 2023 Notes, 2025 Notes and 2028 Notes are based on recent trading prices of the respective instruments.

7. CAPITALIZED FEES PAID

Capitalized fees paid, which consist of registrational and launch-related milestone fees paid to GSK, were as follows:

		December 31,	
(In thousands)	Amortization period	2022	2021
United States	2013-2030	$ 120,000	$ 120,000
Europe	2013-2029	60,000	60,000
Japan	2013-2029	40,000	40,000
Gross carrying value		220,000	220,000
Accumulated amortization		(122,393)	(108,570)
Net carrying value		$ 97,607	$ 111,430

These milestone fees are amortized over their estimated useful lives commencing upon the commercial launch of the product in their respective regions with the amortization recorded as a reduction in revenue from collaborative arrangements. As of December 31, 2022, the weighted average remaining amortization period was 7.1 years.

Additional information regarding these milestone fees is included in Note 3, "Revenue Recognition". Amortization for each of the years ended December 31, 2022, 2021 and 2020 was $13.8 million. The remaining estimated amortization is $13.8 million for each of the years from 2023 to 2027 and $28.6 million thereafter.

8. GOODWILL AND INTANGIBLE ASSETS

Goodwill and intangible assets acquired are recognized at fair value as of the acquisition date. The carrying amount of goodwill as of December 31, 2022 was $26.7 million. We have not recognized any impairment losses related to goodwill and intangible assets during the periods presented.

Intangible assets with definite lives are amortized over their estimated useful lives. The carrying basis and accumulated amortization of recognized intangible assets as of December 31, 2022 were as follows:

(In thousands)	Useful Life (Years)	Gross Amount	Accumulated Amortization	Net Carrying Amount
Marketed products	8-10	$ 151,000	$ (5,581)	$ 145,419
In-process research and development		72,100	—	72,100
Collaboration agreement		35,400	—	35,400
Total		$ 258,500	$ (5,581)	$ 252,919

Intangible assets recognized as a result of the acquisition of Entasis amounted to $107.5 million, which consisted of Entasis' in-process research and development related to its antibacterial therapeutic product candidates and a collaboration agreement amounting to $72.1 million and $35.4 million, respectively. The useful lives of these intangible assets will be determined upon commercialization of the underlying product candidates; thus, no amortization expense of determinable assets was recognized during the year ended December 31, 2022.

Intangible assets recognized as a result of the acquisition of La Jolla amounting to $151.0 million pertain to product rights and developed technologies on La Jolla's currently marketed products. These are intangible assets with determinable lives and are amortized over their estimated useful lives. We recognized amortization expense of $5.6 million for the year ended December 31, 2022. Future amortization expense is expected to be $15.4 million for each of the years from 2023 to 2027 and $68.2 million thereafter.

9. BALANCE SHEET COMPONENTS

Inventory

Inventory consisted of the following:

(In thousands)	December 31, 2022
Raw materials	$ 5,757
Work-in-process	25,052
Finished goods	25,088
Total inventory	$ 55,897

As of December 31, 2022, total inventory included net fair value adjustments resulting from the acquisition of La Jolla of approximately $49.5 million, which will be recognized as cost of products sold when sales occur in future periods. The fair value adjustments recorded as part of cost of products sold amounted to $10.0 million for the year ended December 31, 2022. There was no inventory as of December 31, 2021.

Other Accrued Liabilities

Other accrued liabilities consisted of the following:

	December 31,	
(In thousands)	2022	2021
Accrued contract manufacturing expenses	$ 8,382	$ —
Accrued clinical expenses	692	—
Accrued research expenses	349	—
Accrued professional services	3,977	894
Current portion of lease liabilities	1,316	106
Current portion of deferred royalty obligation	2,639	—
Accrued license fees and royalties	943	—
Other	2,909	9
Total other accrued liabilities	$ 21,207	$ 1,009

Other Long-Term Liabilities

Other long-term liabilities consisted of the following:

(In thousands)	December 31, 2022
Long-term portion of deferred royalty obligation	$ 67,947
Long-term portion of lease liabilities	2,376
Contingent value rights liability	595
Total other long-term liabilities	$ 70,918

There were no other long-term liabilities as of December 31, 2021.

10. STOCK-BASED COMPENSATION

Equity Incentive Plans

In May 2012, we adopted the 2012 Equity Incentive Plan (the "2012 Plan"). The 2012 Plan provides for the grant of incentive stock options, nonstatutory stock options, RSAs, RSUs and Stock Appreciation Rights to employees, non-employee directors and consultants. As of December 31, 2022, total shares remaining available for issuance under the 2012 Plan were 3,838,270.

Employee Stock Purchase Plan

Under the 2004 Employee Stock Purchase Plan (the "ESPP"), our employees may purchase common stock through payroll deductions at a price equal to 85% of the lower of the fair market value of the stock at the beginning of the offering period or at the end of each applicable purchase period. The ESPP provides for consecutive and overlapping offering periods of 24 months in duration, with each offering period composed of four consecutive six-month purchase periods. The purchase periods end on either May 15 or November 15. ESPP contributions are limited to a maximum of 15% of an employee's eligible compensation. The maximum number of shares that an employee may purchase in any purchase period is 2,500. An employee may not purchase shares with a value greater than $25,000 in any calendar year.

As of December 31, 2022, total shares remaining available for issuance under the ESPP were 160,995.

Director Compensation Program

Our non-employee directors receive compensation for services provided as a director. Each member of our board of directors who is not an employee receives both cash and equity compensation for services as a director, member of a committee of the board of directors, lead independent director and chairman, as applicable. In October 2017, both the cash and equity components of the compensation program were amended, effective immediately (the "October 2017 Amendments").

Each of our independent directors receives periodic automatic grants of equity awards under a program implemented under the 2012 Plan. These grants are non-discretionary. Only our independent directors or affiliates of such directors are eligible to receive automatic grants under the 2012 Plan. Under the program, each individual who first became a non-employee director will, on the date such individual joins the board of directors, automatically be granted a one-time grant of RSUs covering a number of shares of our common stock calculated as $125,000 ($250,000 prior to the October 2017 Amendments) divided by our common stock closing share price on the date of grant as reported on The Nasdaq Global Select Market, rounded down to the nearest whole share (the "Initial RSUs"), plus a one-time grant of RSUs covering a number of shares of our common stock calculated as $225,000 ($250,000 prior to the October 2017 Amendments) divided by our common stock closing share price on the date of grant as reported on The Nasdaq Global Select Market, which would be pro-rated for the number of whole months remaining until the anniversary of the prior year's stockholders' meeting, rounded down to the nearest whole share (the "Pro Rata RSUs"). The Initial RSUs vest in two equal annual installments, while Pro Rata RSUs vest in a single installment at the sooner of the next annual stockholder meeting or the one-year grant anniversary, in each case subject to the non-employee director's continuous service through the applicable vesting date.

Annually, upon his or her re-election to the board of directors at the Annual Meeting of Stockholders, each non-employee director is automatically granted an RSU covering a number of shares of our common stock calculated as $225,000 ($250,000 prior to the October 2017 Amendments) divided by our common stock closing share price on the date of grant as reported on The Nasdaq Global Select Market, rounded down to the nearest whole share. These RSUs will vest at the sooner of the next annual stockholder meeting or the one-year anniversary of grant, subject to the non-employee director's continuous service through the applicable vesting date. Following the amendment to our non-employee director compensation program, both the annual RSUs and Initial RSUs described above remained unchanged with the exception that the number of shares of our common stock subject to each award has been reduced.

These RSUs will vest in full upon the director's death, the occurrence of a change in control or, with respect to awards made after the October 2017 Amendments, the director's disability before the director's service terminates. Director RSUs carry dividend equivalent rights to be credited with an amount equal to all cash dividends paid on the underlying shares of common stock while unvested. Dividend equivalents are subject to the same terms and conditions, including vesting, as the RSUs to which they attach and are paid in cash upon vesting.

INNOVIVA, INC.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS (Continued)

Stock-Based Compensation Expense

Stock-based compensation expense is included in the consolidated statements of income as follows:

	Year Ended December 31,		
(In thousands)	2022	2021	2020
Selling, general and administrative	$ 5,305	$ 2,017	$ 1,698
Research and development	2,042	—	—
Total	$ 7,347	$ 2,017	$ 1,698

Stock-based compensation expense included in the consolidated statements of income by award type is as follows:

	Year Ended December 31,		
(In thousands)	2022	2021	2020
Stock options	$ 3,057	$ 490	$ 242
RSUs	4,053	1,280	1,149
RSAs	194	200	273
ESPP	43	47	34
Total stock-based compensation expense	$ 7,347	$ 2,017	$ 1,698

As of December 31, 2022, the unrecognized stock-based compensation cost and the estimated weighted-average amortization period were as follows:

(In thousands)	Unrecognized Compensation Cost	Weighted-Average Amortization Period (Years)
Stock options	$ 3,550	2.9
RSUs	4,776	2.2
RSAs	388	2.6
Total unrecognized compensation expense	$ 8,714	

Compensation Awards

The following table summarizes equity award activity under the 2012 Plan and prior plans and related information:

(In thousands, except per share data)	Number of outstanding options	Weighted-Average Exercise Price of Outstanding Options	Number of outstanding RSUs	Weighted-Average Fair Value per Share at Grant	Number of outstanding RSAs	Weighted-Average Fair Value per Share at Grant
Balance as of December 31, 2021	766	$ 20.79	116	$ 12.82	29	$ 13.35
Granted	492	$ 14.92	676	$ 11.06	15	$ 16.67
Exercised	(15)	$ 17.11	—	$ —	—	$ —
Released RSUs and RSAs	—	$ —	(233)	$ 9.90	(14)	$ 13.51
Forfeited	(295)	$ 28.01	(41)	$ 8.80	—	$ —
Balance as of December 31, 2022	948	$ 15.56	518	$ 12.16	30	$ 14.97
Vested and expected to vest as of December 31, 2022	948	$ 15.56	518	$ 12.16	—	$ —

As of December 31, 2022, the aggregate intrinsic value of options outstanding and options exercisable was not material. As of December 31, 2021, the aggregate intrinsic value of the options outstanding was $1.3 million and the aggregate intrinsic value of options exercisable was immaterial. As of December 31, 2022, 290 options were exercisable. The weighted average remaining contractual term of options outstanding was 8.01 years and 4.43 years as of December 31, 2022 and 2021, respectively.

The total intrinsic value of the options exercised was not material as of December 31, 2022. The total intrinsic value of the options exercised was $0.2 million and $0.1 million for the years ended December 31, 2021 and 2020, respectively. The total estimated fair value of options vested was $0.6 million for the year ended December 31, 2021. The total estimated fair value of options vested was not material for the year ended December 31, 2022 and 2020, respectively.

The total estimated fair value of RSUs vested was $2.3 million, $1.1 million and $1.3 million for the year December 31, 2022, 2021 and 2020.

The total estimated fair value of RSAs vested was not material for the year ended December 31, 2022, 2021, and 2020.

Valuation Assumptions

The weighted-average assumptions used in calculating the estimated value of our stock options on the date of grant as follows:

	Year Ended December 31,		
	2022	2021	2020
Risk-free interest rate	3.6%	1.1%	0.4%
Expected term (in years)	6.04	6.11	6.11
Volatility	38.6%	44.9%	46.9%
Dividend yield	0.0%	0.0%	0.0%
Weighted-average estimated fair value of stock options granted	$ 6.43	$ 5.84	$ 6.28

11. STOCKHOLDERS' EQUITY

On October 31, 2022, our board of directors authorized a new share repurchase program under which we may repurchase up to $100.0 million of our outstanding shares of common stock. The timing and amount of any share repurchases under the share repurchase program will be determined by our management in its discretion based on ongoing assessments of the capital needs of the business, the market price of our common stock, prevailing stock prices, general market conditions and other considerations. Share repurchases under the program may be made through a variety of methods, which may include open market purchases, privately negotiated transactions, in block trades, accelerated share repurchase transactions, exchange transactions, or any combination thereof or by other means in accordance with federal securities laws. This program has no termination date, may be suspended or discontinued at any time at our discretion, and does not obligate us to acquire any amount of common stock. As of December 31, 2022, we have repurchased 647,394 shares in the open market at an average price of $13.13 per share for a total amount of approximately $8.5 million. Subsequent to December 31, 2022 and through February 24, 2023, we have repurchased 1,522,947 shares in the open market at an average price of $12.63 per share for a total amount of approximately $19.2 million. All the repurchased shares were retired.

12. DEBT

Our debt consists of:

	December 31,	
(In thousands)	2022	2021
2023 Notes	$ 96,204	$ 240,984
2025 Notes	192,500	192,500
2028 Notes	261,000	—
Total debt	549,704	433,484
Less: Unamortized debt discount and issuance costs	(9,331)	(38,831)
Total debt, net	540,373	394,653
Less: Current portion of long-term debt, net	96,193	—
Total long-term debt, net	$ 444,180	$ 394,653

Convertible Subordinated Notes Due 2023

In January 2013, we completed an underwritten public offering of $287.5 million aggregate principal amount of unsecured convertible subordinated notes, with maturity date of January 15, 2023. The financing raised proceeds, net of issuance costs, of approximately $281.2 million, less $36.8 million to purchase two privately negotiated capped call option transactions in connection

with the issuance of the notes. The 2023 Notes bear interest at the rate of 2.125% per year that is payable semi-annually in arrears in cash on January 15 and July 15 of each year, beginning on July 15, 2013.

The 2023 Notes were convertible, at the option of the holder, into shares of our common stock at an initial conversion rate of 35.9903 shares per $1,000 principal amount of the 2023 Notes, subject to adjustment in certain circumstances, which represents an initial conversion price of approximately $27.79 per share.

In connection with the offering of the 2023 Notes, we entered into two privately negotiated capped call option transactions with a single counterparty. The capped call option transaction is an integrated instrument consisting of a call option on our common stock purchased by us with a strike price equal to the initial conversion price of $27.79 per share for the underlying number of shares and a cap price of $38.00 per share, both of which are subject to adjustments consistent with the 2023 Notes. The cap component is economically equivalent to a call option sold by us for the underlying number of shares with an initial strike price of $38.00 per share. As an integrated instrument, the settlement of the capped call coincides with the due date of the convertible debt. Upon settlement, we would receive from our hedge counterparty a number of shares of our common shares that would range from zero, if the stock price was below $27.79 per share, to a maximum of 2,779,659 shares, if the stock price is above $38.00 per share. However, if the market price of our common stock, as measured under the terms of the capped call transactions, exceeds $38.00 per share, there is no incremental anti-dilutive benefit from the capped call.

As a result of the partial conversion by certain holders of the 2023 Notes in July 2014, and dividends declared and paid in 2014 and 2015, the conversion rate with respect to our 2023 Notes was adjusted in total to 50.5818 shares of our common stock per $1,000 principal amount of the 2023 Notes, which represents a conversion price of approximately $19.77 per share. As a result of the conversion rate adjustments, the capped call strike price and cap price were also adjusted to $19.77 and $27.04, respectively.

For the year ended December 31, 2016, we retired a portion of our 2023 Notes with a face value of $14.1 million and carrying value of $13.9 million by way of purchase in the open market.

On March 7, 2022, we used $165.6 million from the sale of the 2028 Notes to repurchase 60% of the 2023 Notes with a face value of $144.8 million. The carrying value of the repurchased 2023 Notes was $144.5 million. Accrued interest was $0.4 million and unamortized debt issuance costs were $0.3 million on the date of repurchase. We recognized a loss on the extinguishment of the 2023 Notes of $20.7 million in other expense, net, in the consolidated statement of operations. The repurchase reduced the outstanding principal balance to $96.2 million and unamortized debt issuance costs to $0.2 million. The annual effective interest rate of the 2023 Notes changed from 2.36% to 2.37%.

On April 18, 2022, certain 2023 Notes holders converted their notes of $3.0 thousand into Innoviva's common stock. The outstanding principal balance was reduced slightly to $96.2 million.

Our outstanding 2023 Notes balances consisted of the following:

	December 31,	
(In thousands)	2022	2021
Principal	$ 96,204	$ 240,984
Debt issuance costs, net	(11)	(620)
Net carrying amount	$ 96,193	$ 240,364

The following table sets forth total interest expense recognized related to the 2023 Notes for the years ended December 31, 2022, 2021 and 2020:

	Year Ended December 31,		
(In thousands)	2022	2021	2020
Contractual interest expense	$ 2,617	$ 5,121	$ 5,121
Amortization of debt issuance costs	302	580	567
Total interest and amortization expense	$ 2,919	$ 5,701	$ 5,688

The 2023 Notes were fully paid upon their maturity date in January 2023.

Convertible Senior Notes Due 2025

On August 7, 2017, we completed a private placement of $192.5 million aggregate principal amount of our 2025 Notes. The proceeds include the 2025 Notes sold pursuant to the $17.5 million over-allotment option granted by us to the initial purchasers, which option was exercised in full. The 2025 Notes were sold in a private placement to qualified institutional buyers pursuant to Rule 144A under the Securities Act. The 2025 Notes are senior unsecured obligations and bear interest at a rate of 2.5% per year, payable semi-annually in arrears on February 15 and August 15 of each year, beginning on February 15, 2018.

The 2025 Notes are convertible, based on the applicable conversion rate, into cash, shares of our common stock or a combination thereof, at our election. The initial conversion rate for the 2025 Notes is 57.9240 shares of our common stock per $1,000 principal amount of the 2025 Notes (which is equivalent to an initial conversion price of approximately $17.26 per share), representing a 30.0% conversion premium over the last reported sale price of the Company's common stock on August 1, 2017, which was $13.28 per share. The conversion rate is subject to customary anti-dilution adjustments in certain circumstances. The 2025 Notes will mature on August 15, 2025, unless repurchased or converted in accordance with their terms prior to such date. Prior to February 15, 2025, the 2025 Notes will be convertible at the option of the holders only upon the occurrence of specified events and during certain periods. From, and including, February 15, 2025, until the close of business on the second scheduled trading day immediately preceding the maturity date, the 2025 Notes will be convertible at any time.

Holders of the 2025 Notes may convert all or a portion of their 2025 Notes prior to the close of business on February 15, 2025 only under the following circumstances:

- after September 30, 2017, if our closing common stock price for at least 20 days out of the most recent 30 consecutive trading days of the preceding quarter is greater than 130% of the current conversion price of the 2025 Notes;
- for five consecutive business days, if the average trading price per $1,000 of Notes during the prior 10 consecutive trading days is less than 98% of the product of our closing common stock price and the conversion rate of the 2025 Notes on such day; and,
- upon the occurrence of specified corporate events, including certain distributions, the occurrence of a fundamental changes (as defined in the indenture governing the 2025 Notes) or a transaction resulting in our common stock converting into other securities or property or assets.

On or after February 15, 2025, holders of the 2025 Notes may convert their 2025 Notes at any time until the close of business on the second scheduled trading day immediately preceding the maturity date of the 2025 Notes.

In the event of default or a fundamental change (as defined above), holders of the 2025 Notes may require us to repurchase all or a portion of their 2025 Notes at price equal to 100% of the principal amount of the 2025 Notes, plus any accrued and unpaid interest.

Effective January 1, 2022, we adopted ASU 2020-06 using a modified retrospective method, under which financial results reported in prior periods were not adjusted. The adoption of ASU 2020-06 had a material impact on the 2025 notes. Refer to Note 1, "Description of Operations and Summary of Significant Accounting Policies", for further information.

Prior to the adoption of ASU 2020-06, we separately accounted for the liability and equity components of the 2025 Notes by allocating the proceeds between the liability component and the embedded conversion option ("equity component") due to our ability to settle the conversion obligation of the 2025 Notes in cash, common stock or a combination of cash and common stock, at our option. The carrying amount of the liability component was calculated by measuring the fair value of a similar liability that does not have an associated convertible feature using the income approach. The allocation was performed in a manner that reflected our non-convertible debt borrowing rate for similar debt. The equity component of the 2025 Notes of $67.3 million was recognized as a debt discount and represents the difference between the proceeds from the issuance of the 2025 Notes and the fair value of the liability of the 2025 Notes on the date of issuance. The excess of the principal amount of the liability component over its carrying amount ("debt discount") was amortized to interest expense using the effective interest method over the term of the 2025 Notes. The equity component was not remeasured as long as it continued to meet the conditions for equity classification. Additionally, we separated the total issuance costs of $5.4 million incurred into liability and equity components in proportion to the allocation of the initial proceeds, resulting in liability issuance costs of $3.5 million and equity issuance costs of $1.9 million. Issuance costs attributable to the liability

component were amortized on a straight-line basis, which approximated the effective interest rate method, to interest expense over the term of the 2025 Notes. The issuance costs attributable to the equity component were netted against the equity component in additional paid-in capital. The annual effective interest rate of the liability component of the 2025 Notes was 8.87%.

Upon adoption of ASU 2020-06 on January 1, 2022, we combined the liability and equity components of the 2025 Notes assuming that the instrument was accounted for as a single liability from inception to the date of adoption. We similarly combined the liability and equity components of the issuance costs. The issuance costs are presented as a deduction from the outstanding principal balance of the 2025 Notes and are amortized on a straight-line basis over the term of the 2025 Notes under the effective interest rate method. As of January 1, 2022, the annual effective interest rate on the 2025 Notes was 2.88%.

Our outstanding 2025 Notes balances consisted of the following:

	December 31,	
(In thousands)	2022	2021
Liability component		
Principal	$ 192,500	$ 192,500
Debt discount and issuance costs, net	(1,917)	(38,211)
Net carrying amount	$ 190,583	$ 154,289
Equity component, net	$ —	$ 65,361

The following table sets forth total interest expense recognized related to the 2025 Notes for the years ended December 31, 2022, 2021 and 2020:

	Year Ended December 31,		
(In thousands)	2022	2021	2020
Contractual interest expense	$ 4,813	$ 4,813	$ 4,813
Amortization of debt issuance costs	692	657	601
Amortization of debt discount	—	7,898	7,230
Total interest and amortization expense	$ 5,505	$ 13,368	$ 12,644

Convertible Senior Notes Due 2028

In March 2022, we completed a private placement of $261.0 million aggregate principal amount of our 2028 Notes, which will mature on March 15, 2028. The proceeds include the 2028 Notes sold pursuant to the $45.0 million over-allotment option granted by us to the initial purchasers, of which $36.0 million was exercised. The 2028 Notes were sold in a private placement to qualified institutional buyers pursuant to Rule 144A under the Securities Act.

The net proceeds from the sale of the $261.0 million aggregate principal amount of 2028 Notes were approximately $252.6 million after deducting the initial purchasers' discounts and commissions and our estimated offering expenses. We used approximately $21.0 million of the net proceeds from the offering to fund the cost of entering into the capped call transactions described below. In addition, we used $165.6 million of the remaining net proceeds to repurchase $144.8 million aggregate principal amount of the 2023 Notes in separate and individually negotiated transactions with certain holders of the 2023 Notes, which closed concurrently with the issuance of the 2028 Notes. We expect to use the remaining net proceeds for general corporate purposes.

The 2028 Notes bear interest at an annual rate of 2.125% that is payable semi-annually in arrears in cash on March 15 and September 15 of each year, beginning on September 15, 2022.

The 2028 Notes are convertible, based on the applicable conversion rate, into cash, shares of our common stock or a combination thereof, at our election. The initial conversion rate was 38.1432 shares per $1,000 principal amount of the 2028 Notes, subject to customary anti-dilution adjustment in certain circumstances, which represented an initial conversion price of approximately $26.22 per share.

Prior to September 15, 2027, the 2028 Notes will be convertible at the option of the holders only upon the occurrence of specified events and during certain periods, and will be convertible on or after September 15, 2027, at any time until the close of business on the second scheduled trading day immediately preceding the maturity date of the 2028 Notes.

Holders of the 2028 Notes may convert all or a portion of their 2028 Notes prior to the close of business on September 15, 2027, only under the following circumstances:

- after March 31, 2022, if our closing common stock price for at least 20 days out of the most recent 30 consecutive trading days of the preceding quarter is greater than 130% of the current conversion price of the 2028 Notes;
- for five consecutive business days, if the average trading price per $1,000 of Notes during the prior 10 consecutive trading days is less than 98% of the product of our closing common stock price and the conversion rate of the 2028 Notes on such day; and,
- upon the occurrence of specified corporate events, including certain distributions, the occurrence of a fundamental changes (as defined in the indenture governing the 2028 Notes) or a transaction resulting in our common stock converting into other securities or property or assets.

On or after September 15, 2027, holders of the 2028 Notes may convert their 2028 Notes at any time until the close of the business on the second day immediately preceding the maturity date of the 2028 Notes.

The 2028 Notes will be redeemable, in whole or in part, at our option at any time, and from time to time, on or after March 20, 2025, and on or before the 75th scheduled trading day immediately before the maturity date but only if the last reported sale price per share of our common stock exceeds 130% of the conversion price for a specified period of time. The redemption price will be equal to the principal amount of the 2028 Notes to be redeemed, plus accrued and unpaid interest, if any, to, but excluding, the redemption date. In addition, calling any 2028 Note for redemption will constitute a make-whole fundamental change (as defined in the indenture governing the 2028 Notes) with respect to that 2028 Note, in which case the conversion rate applicable to the conversion of that 2028 Note will be increased in certain circumstances if it is converted after it is called for redemption.

If we undergo a fundamental change, subject to certain conditions, holders may require us to purchase for cash all or any portion of their 2028 Notes. The fundamental change purchase price will be 100% of the principal amount of the 2028 Notes to be purchased plus any accrued and unpaid interest to, but excluding, the fundamental change purchase date.

The indenture governing the 2028 Notes contains customary terms and covenants, including a merger covenant and that upon certain events of default occurring and continuing, either the Trustee or the holders of at least 25% of the aggregate principal amount of the outstanding Notes may declare 100% of the principal of, and accrued and unpaid interest, if any, on, all the Notes to be due and payable immediately.

In connection with the offering of the 2028 Notes, we entered into privately negotiated capped call transactions. The cap price of the capped call transaction is initially $33.9850 per share and is subject to certain adjustments under the terms of the capped call transactions. The capped call transactions cover, subject to customary adjustments, the number of shares of common stock initially underlying the 2028 Notes. The capped call transactions are expected generally to reduce potential dilution to our common stock upon conversion of the 2028 Notes or at our election (subject to certain conditions) offset any cash payments we are required to make in excess of the aggregate principal amount of converted 2028 Notes, as the case may be, with such reduction or offset subject to a cap.

The annual effective interest rate on the 2028 Notes is 2.70%.

Our outstanding 2028 Notes balance consisted of the following:

(In thousands)	December 31, 2022
Liability component	
Principal	$ 261,000
Debt discount and issuance costs, net	(7,403)
Net carrying amount	$ 253,597

The following table sets forth total interest expense recognized related to the 2028 Notes from the issuance through December 31, 2022:

(In thousands)	Date of Issuance through December 31, 2022
Contractual interest expense	$ 4,514
Amortization of debt issuance costs	1,061
Total interest and amortization expense	$ 5,575

Debt Maturities

The aggregate scheduled maturities of our long-term debt as of December 31, 2022 are as follows:

(In thousands)	Amount
Year ending December 31,	
2023	$ 96,204
2024	—
2025	192,500
2026	—
2027	—
Thereafter	261,000
Total	$ 549,704

Deferred Royalty Obligation

As part of our acquisition of La Jolla, we recorded the fair value of its deferred royalty obligation in connection with La Jolla's royalty financing agreement ("La Jolla Royalty Agreement") with HealthCare Royalty Partners ("HCR"). Under the terms of the La Jolla Royalty Agreement, HCR is entitled to receive quarterly royalties on worldwide net sales of GIAPREZA® until either January 1, 2031 or when the maximum aggregate royalty payments have been made, whichever occurs first. Quarterly payments to HCR under the Royalty Agreement start at a maximum royalty rate, with step-downs based on the achievement of annual net product sales thresholds. The current maximum royalty rate is 14%. Starting January 1, 2024, the maximum royalty rate may increase by an additional 4%, if an agreed-upon, cumulative net product sales threshold has not been met. The La Jolla Royalty Agreement is subject to maximum aggregate royalty payments to HCR of $225.0 million.

From the date of our acquisition of La Jolla through December 31, 2022, we recognized interest expense of $1.8 million on the deferred royalty obligation. The carrying value of the deferred royalty obligation and accrued interest as of December 31, 2022 was $70.6 million, $67.9 million of which was classified as part of other long-term liabilities on the consolidated balance sheet and the remaining $2.7 million was classified as other accrued liabilities on the consolidated balance sheet. From the date of acquisition of La Jolla through December 31, 2022, we made royalty payments to HCR of $1.0 million. The deferred royalty obligation was valued using Level 3 inputs, and its carrying value as of December 31, 2022 approximates fair value. The fair value of the deferred royalty obligation was calculated as the discounted deferred royalty obligations based on risk-adjusted revenue projections for GIAPREZA®. The annual effective interest rate of the deferred royalty obligation was 7.34%.

Under the terms of the La Jolla Royalty Agreement, if we are unable to meet certain obligations, including the obligation to use commercially reasonable and diligent efforts to commercialize GIAPREZA®, HCR would have the right to terminate the La Jolla Royalty Agreement and demand payment of either $125.0 million or $225.0 million (depending on which obligation we have failed to meet) less aggregate royalties already paid to HCR. As of December 31, 2022, inclusive of the aggregate royalties paid to HCR by La Jolla under the La Jolla Royalty Agreement prior to our acquisition, La Jolla paid $12.7 million of aggregate royalties to HCR. In the event that we fail to pay such amount if and when due in a timely manner, HCR would have the right to foreclose on the GIAPREZA®-related assets. HCR has no recourse against any asset other than GIAPREZA®.

Certain contract provisions within the La Jolla Royalty Agreement that could result in an acceleration of amounts due under the La Jolla Royalty Agreement are recognized as embedded derivatives that require bifurcation from the deferred royalty obligation and fair value recognition. We determined the fair value of each derivative by assessing the probability of each event occurring, as well as the potential repayment amounts and timing of such repayments that would result under various scenarios. As a result of this assessment, we determined that the fair value of the embedded derivatives is not material and, therefore, not recognized as of December 31, 2022. We estimate the fair value of the embedded derivatives for each reporting period until either the features lapse or the La Jolla Royalty Agreement is terminated, whichever occurs first. Any material change in the fair value of the embedded derivatives will be recorded as either a gain or loss on the consolidated statements of income.

13. COMMITMENTS AND CONTINGENCIES

Operating Lease

We have operating leases for our corporate headquarters, office spaces and laboratory facilities.

Our operating leases include a facility lease consisting of 20,062 square feet of office and laboratory space in Waltham, Massachusetts. Effective April 2022, we exercised our renewal option for to extend the lease term for three additional years through December 2025.

In 2019, we entered into an operating lease for our headquarters in Burlingame, California for approximately 2,111 rentable square feet. The lease commenced in November 2019 with a term of thirty-six calendar months, which was subsequently amended to expire in December 2023.

The components of lease costs are as follows:

(In thousands)	Year Ended December 31, 2022
Straight line operating lease costs	$ 1,585
Variable lease costs	155
Total lease costs	$ 1,740

Supplemental cash flow information related to leases are as follows:

(In thousands)	Year Ended December 31, 2022
Cash paid for amounts included in the measurement of operating lease liabilities:	$ 790
Operating lease right-of-use assets obtained in exchange for operating lease obligations	3,323
Right-of-use assets obtained through acquisitions	1,185

As of December 31, 2022, our operating leases have a weighted-average remaining lease term of 2.8 years and the weighted-average incremental borrowing rate used to determine the operating lease right-of-use assets and lease liabilities was 7.5%.

We have not presented the comparative information above for the years ended December 31, 2021 and 2020 as our operating lease during those years was not material.

The following table summarizes our operating leases as presented on the consolidated balance sheets:

(In thousands)	December 31, 2022	December 31, 2021
Assets		
Right-of-use assets	$ 3,265	$ 97
Liabilities		
Current portion of lease liabilities included within Other accrued liabilities	$ 1,316	$ 106
Long-term portion of lease liabilities included within Other long-term liabilities	2,376	—
Total lease liabilities	$ 3,692	$ 106

Future minimum lease payments on our operating leases as of December 31, 2022 are as follows:

(In thousands)	Amount
Year ending December 31,	
2023	$ 1,542
2024	1,269
2025	1,289
Total undiscounted lease payments	4,100
Less: imputed interest	(408)
Total operating lease liabilities	$ 3,692

Legal Proceedings

From time to time, the Company is involved in legal proceedings in the ordinary course of its business. We are not currently a party to any material legal proceedings except as discussed below.

On February 15, 2022, La Jolla received a paragraph IV notice of certification (the "Notice Letter") from Gland Pharma Limited ("Gland") advising that Gland had submitted an Abbreviated New Drug Application ("ANDA") to the FDA seeking approval to manufacture, use or sell a generic version of GIAPREZA® in the U.S. prior to the expiration of U.S. Patent Nos.: 9,220,745; 9,572,856; 9,867,863; 10,028,995; 10,335,451; 10,493,124; 10,500,247; 10,548,943; 11,096,983; and 11,219,662 (the "GIAPREZA® Patents"), which are listed in the FDA's Approved Drug Products with Therapeutic Equivalence Evaluations (the "Orange Book"). The Notice Letter alleges that the GIAPREZA® Patents are invalid, unenforceable and/or will not be infringed by the commercial manufacture, use or sale of the generic product described in Gland's ANDA.

On March 29, 2022, La Jolla filed a complaint for patent infringement of the GIAPREZA® Patents against Gland and certain related entities in the United States District Court for the District of New Jersey in response to Gland's ANDA filing. In accordance with the Hatch-Waxman Act, because GIAPREZA® is a new chemical entity and La Jolla filed a complaint for patent infringement within 45 days of receipt of the Notice Letter, the FDA cannot approve Gland's ANDA any earlier than 7.5 years from the approval of the GIAPREZA® NDA unless the District Court finds that all of the asserted claims of the patents-in-suit are invalid, unenforceable and/or not infringed. We intend to vigorously enforce our intellectual property rights relating to GIAPREZA®.

Given the early stage of this matter, we cannot reasonably estimate a potential future loss or a range of potential future losses, if any, and have not recorded a contingent liability accrual as of December 31, 2022.

Indemnifications and Other Contingencies

In the ordinary course of business, we may provide indemnifications of varying scope and terms to vendors, directors, officers, and other parties with respect to certain matters, including, but not limited to, losses arising out of breach of such agreements, services to be provided by us, our negligence or willful misconduct, violations of law, or intellectual property infringement claims made by

third parties. In addition, we have entered into indemnification agreements with directors and certain officers and employees that will require us, among other things, to indemnify them against certain liabilities that may arise by reason of their status or service as directors, officers, or employees. No material demands have been made upon us to provide indemnification under such agreements, and thus, there are no claims that we are aware of that could have a material effect on our consolidated financial statements. We also maintain director and officer insurance, which may cover certain liabilities arising from our obligation to indemnify our directors. To date, we have not incurred any material costs and, as of December 31, 2022, we have not accrued any liabilities in the consolidated financial statements as a result of these provisions.

14. INCOME TAXES

Income tax expense consists of the following:

	Year Ended December 31,		
(In thousands)	2022	2021	2020
Current			
Federal	$ 40,822	$ —	$ —
State	464	7	11
Total current	41,286	7	11
Deferred			
Federal	26,026	70,893	60,408
State	(625)	5,539	12
Total deferred	25,401	76,432	60,420
Total income tax expense, net	$ 66,687	$ 76,439	$ 60,431

The impacts of the differences between the expected U.S. federal statutory income tax to our income tax expense are as follows:

	Year Ended December 31,		
(In thousands)	2022	2021	2020
Expected tax at federal statutory rate	$ 58,928	$ 93,507	$ 74,392
State income tax, net of federal benefit	(1,414)	848	(26)
Federal and state research credits	(2,453)	1,260	—
Noncontrolling interest	7,468	(21,626)	(14,577)
Impact of consolidation and deconsolidation of subsidiaries	(8,897)	—	—
Other	(125)	1,129	839
Change in valuation allowance	13,180	1,321	(197)
Income tax expense (benefit), net	$ 66,687	$ 76,439	$ 60,431

Deferred income taxes reflect the net tax effects of temporary differences between the carrying amounts of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes. Significant components of our deferred tax assets and deferred tax liabilities are as follows:

	December 31,	
(In thousands)	2022	2021
Deferred tax assets		
Net operating loss carryforwards	$ 149,646	$ 64,813
Research and development tax credit carryforwards	21,230	53,467
Unrealized loss on investment, net	6,032	—
Deferred royalty obligation, net	17,404	—
Other	8,527	743
Total deferred tax assets before valuation allowance	202,839	119,023
Valuation allowance	(144,808)	(64,744)
Total deferred tax assets	58,031	54,279
Deferred tax liabilities		
Depreciation and amortization	(50,587)	(9,158)
Unrealized gain on investment, net	—	(27,794)
Inventory fair value adjustment	(12,410)	—
Other	(805)	—
Net deferred tax assets (liabilities)	$ (5,771)	$ 17,327

We record deferred tax assets if the realization of such assets is more likely than not to occur. Significant management judgment is required in determining whether a valuation allowance against the deferred tax assets is required. We have considered all available evidence, both positive and negative, such as our historical operating results and predictability of future taxable income, in making such determination. We are also required to exercise significant management's judgment in forecasting future taxable income. Specifically, we evaluate the following criteria when considering a valuation allowance:

- the history of tax net operating losses in recent years;
- predictability of operating results;
- profitability for a sustained period of time; and
- level of profitability on a quarterly basis.

As of December 31, 2022, we had federal net operating loss carryforwards of approximately $411.5 million, which will expire beginning 2032. As of December 31, 2022, we also had state net operating loss carryforwards of approximately $955.3 million, which will expire beginning 2029 and state research tax credits of approximately $33.3 million, which do not expire.

Utilization of net operating loss and tax credit carryforwards may be subject to a substantial annual limitation due to ownership change limitations provided by the Internal Revenue Code and similar state provisions. Annual limitations may result in expiration of net operating loss and tax credit carryforwards before some or all of such amounts have been utilized.

We conducted an Internal Revenue Code of 1986, as amended, Section 382 ("Section 382") analysis of the Company through December 31, 2022 to determine whether an ownership change had occurred since inception. The Section 382 study concluded that it is more likely than not that the Company did not experience an ownership change during the testing period. However, notwithstanding the applicable annual limitations, no portion of our net operating loss or credit carryforwards is expected to expire before becoming available to reduce federal and state income tax liabilities as a result of those identified ownership changes. If we undergo another ownership change, the utilization of the pre-ownership change net operating loss carryforwards or pre-ownership change tax attributes, such as research tax credits, to offset the post-ownership change income may be subject to an annual limitation, pursuant to Sections 382 and 383 of the Internal Revenue Code of 1986, as amended. Similar rules may apply under state tax laws.

As a result of the acquisition of Entasis, we conducted a study of Entasis' ownership changes and estimated that we will be able to utilize $157.4 million of its federal net operating losses, which are subject to annual limitations.

As a result of the acquisition of La Jolla, we also performed a preliminary analysis of its ownership changes and estimated that we will be able to utilize $254.0 million of its federal net operating losses, which are subject to annual limitations.

Our policy is to recognize interest and/or penalties related to income tax matters in income tax expense. As of December 31, 2022 and 2021, we had no accrued interest or penalties due to the Company's net operating losses available to offset any tax adjustments.

Uncertain Tax Positions

A reconciliation of the beginning and ending balances of the total amounts of unrecognized tax benefits are as follows:

(In thousands)	Amount
Unrecognized tax benefits as of December 31, 2019	$ 15,342
Net decrease in tax portions for 2020	(157)
Unrecognized tax benefits as of December 31, 2020	15,185
Net decrease in tax portions for 2021	(313)
Unrecognized tax benefits as of December 31, 2021	14,872
Net increase in tax portions for 2022	1,452
Unrecognized tax benefits as of December 31, 2022	$ 16,324

We are subject to taxation in the U.S. and various state jurisdictions. The tax years 2004 through 2013, 2015 and forward remain open to examination by the federal and most state tax authorities due to net operating loss and overall credit carryforward positions.

15. SUBSEQUENT EVENTS

On January 10, 2023, we entered into a Secured Convertible Credit Agreement (the "Credit Agreement") with Armata, under which we extended a one-year term loan facility in an aggregate amount of $30.0 million at an interest rate of 8.0% per annum. Pursuant to the Credit Agreement, the balance on the loan, including all accrued and unpaid interest thereon, will convert into shares of Armata's common stock upon the occurrence of a qualified financing, as defined in the Credit Agreement. Any portion of the balance on the loan, including all accrued and unpaid interest thereon, may also be converted into shares of Armata's common stock at our option once a registration statement covering the resale of such securities has been declared effective by the SEC. The loan is secured by substantially all of the assets of Armata and its domestic and foreign material subsidiaries.

On February 2, 2023, ITH entered into a Note Amendment Agreement (the "Note Amendment Agreement") with Gate to amend the Convertible Promissory Note Purchase Agreement entered into in November 2021 between TRC and Gate to acquire the Gate Convertible Note (refer to Note 6, "Equity and Long-Term Investments and Fair Value Measurements"). Pursuant to the Note Amendment Agreement, the principal amount of the Gate Convertible Note was increased from $15.0 million to $21.5 million, which represents the original principal and accrued interests as of the amendment date. All other material terms of the Gate Convertible Note were unchanged.

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Stockholders and the Board of Directors of Innoviva, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheet of Innoviva, Inc. and subsidiaries (the "Company") as of December 31, 2022, the related consolidated statements of income, comprehensive income, stockholders' equity, and cash flows, for the year ended December 31, 2022, and the related notes (collectively referred to as the "financial statements"). In our opinion, the financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2022, and the results of its operations and its cash flows for the year ended December 31, 2022, in conformity with accounting principles generally accepted in the United States of America.

We have also audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the Company's internal control over financial reporting as of December 31, 2022, based on criteria established in *Internal Control — Integrated Framework (2013)*issued by the Committee of Sponsoring Organizations of the Treadway Commission and our report dated February 28, 2023, expressed an unqualified opinion on the Company's internal control over financial reporting.

Change in Accounting Principle

As discussed in Note 1 to the financial statements, effective January 1, 2022, the Company adopted Accounting Standards Update 2020-06, *Debt-Debt with Conversion and Other Options (Subtopic 470-20) and Derivatives and Hedging-Contracts in Entity's Own Equity (Subtopic 815-40): Accounting for Convertible Instruments and Contracts in an Entity's Own Equity*, using the modified retrospective approach.

Basis for Opinion

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's financial statements based on our audit. We are a public accounting firm registered with the PCAOB and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audit in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. Our audit included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audit provides a reasonable basis for our opinion.

Critical Audit Matter

The critical audit matter communicated below is a matter arising from the current-period audit of the financial statements that was communicated or required to be communicated to the audit committee and that (1) relates to accounts or disclosures that are material to the financial statements and (2) involved our especially challenging, subjective, or complex judgments. The communication of critical audit matters does not alter in any way our opinion on the financial statements, taken as a whole, and we are not, by communicating the critical audit matter below, providing a separate opinion on the critical audit matter or on the accounts or disclosures to which it relates.

Consolidated Entities and Equity and Long-term Investments – Primary Beneficiary Determination for Variable Interest Entities – Refer to Notes 1, 5, and 6 to the consolidated financial statements

Critical Audit Matter Description

The Company invests in equity and debt securities of private and public companies. The Company evaluates its interests in these entities to determine whether they meet the definition of a variable interest entity (VIE) or a voting interest entity (VOE) and whether the Company is required to consolidate these entities. A VIE is consolidated by its primary beneficiary, which is the party that has both 1) the power to direct the activities that most significantly impact the economic performance of the VIE and 2) a variable interest that absorbs losses or receives benefits from the VIE that could potentially be significant to the VIE. To determine whether a variable

interest that the Company holds could potentially be significant to the VIE, the Company considers both qualitative and quantitative factors regarding the nature, size and form of the Company's involvement with the VIE. In general, the parties that make the most significant decisions affecting the VIE (management and representation on the Board of Directors) and have the right to unilaterally remove those decision-makers are deemed to have the power to direct the activities of a VIE. The Company will reconsider whether an entity is a VIE and whether the Company is the primary beneficiary of the entity upon the occurrence of certain types of events. The determination of the primary beneficiary of a VIE requires significant management judgment. As of December 31, 2022, the carrying values of the Company's consolidated VIEs' total assets and total liabilities were $320.6 million and $1.6 million, respectively. Additionally, as of December 31, 2022 the carrying value of the Company's investments in unconsolidated VIEs was $377.9 million.

We identified the primary beneficiary determination for the Company's VIEs as a critical audit matter due to the complexity of the accounting principles related to the determination of the primary beneficiary of a VIE and the significant judgment required by management in evaluating the Company's role in establishing the VIE, their ongoing rights and responsibilities and identifying which party, if any, has power over those activities. This required a high degree of auditor judgment and an increased extent of effort, including the involvement of professionals with consolidation accounting expertise, when performing audit procedures to evaluate the Company's determination of whether it is the primary beneficiary for its VIEs.

How the Critical Audit Matter Was Addressed in the Audit

Our audit procedures related to the primary beneficiary determination for VIEs included the following, among others:

- We tested the effectiveness of controls over the Company's primary beneficiary determination for its VIEs, including management's determination of the party that has the power to direct the activities that most significantly impact the economic performance of the VIE and a variable interest that absorbs losses or receives benefits from the VIE that could potentially be significant to the VIE.
- We evaluated the appropriateness of the Company's accounting conclusions for consolidated and unconsolidated VIEs through the following:
    - Evaluated the investment structures and terms of the agreements, including reading the purchase agreements and other related documents which govern the formation and activities of the entity (the Contractual Arrangements).
    - Tested whether the Company appropriately determined the primary beneficiary by evaluating the Contractual Arrangements of the entity to determine if the Company has the power to direct activities that most significantly impact the economic performance of the VIE, and if the Company has the obligation to absorb losses of the entity or the right to receive benefits from the entity that could be significant to the VIE.
    - For certain VIEs, with the assistance of professionals with expertise in consolidation accounting, evaluated the appropriateness of the Company's determination of the primary beneficiary of the VIE.
    - Evaluated the Company's disclosures related to the primary beneficiary determination of its consolidated entities and unconsolidated VIEs.

/s/ Deloitte & Touche LLP

San Jose, California
February 28, 2023

We have served as the Company's auditor since 2022.

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Stockholders and Board of Directors of Innoviva, Inc.

Opinion on the financial statements
We have audited the accompanying consolidated balance sheet of Innoviva, Inc. (a Delaware corporation) and subsidiaries (the "Company") as of December 31, 2021, the related consolidated statements of income, comprehensive income, changes in stockholders' equity, and cash flows for each of the two years in the period ended December 31, 2021, and the related notes (collectively referred to as the "financial statements"). In our opinion, the financial statements present fairly, in all material respects, the financial position of the Company as of December 31, 2021, and the results of its operations and its cash flows for each of the two years in the period ended December 31, 2021, in conformity with accounting principles generally accepted in the United States of America.

Basis for opinion
These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's financial statements based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) ("PCAOB") and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.
We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ GRANT THORNTON LLP

We served as the Company's auditor from 2019 to 2021.

San Francisco, California
February 28, 2022

ITEM 9. CHANGES IN AND DISAGREEMENTS WITH ACCOUNTANTS ON ACCOUNTING AND FINANCIAL DISCLOSURE

None.

ITEM 9A. CONTROLS AND PROCEDURES

Evaluation of Disclosure Controls and Procedures.

We conducted an evaluation as of December 31, 2022, under the supervision and with the participation of our management, including our chief executive officer and chief accounting officer, of the effectiveness of the design and operation of our disclosure controls and procedures, which are defined under SEC rules as controls and other procedures of a company that are designed to ensure that information required to be disclosed by a company in the reports that it files under the Securities Exchange Act of 1934 (Exchange Act) is recorded, processed, summarized and reported within required time periods specified in the Commission's rules and forms and controls and procedures that are designed to ensure that information required to be disclosed by an issuer in the reports that it files or submits under the Exchange Act is accumulated and communicated to the issuer's management including its principal executive and principal financial officers, or persons performing similar functions, as appropriate to allow timely decision regarding required disclosure. Based upon that evaluation, our principal executive officer and principal financial officer concluded that, as of such date, our disclosure controls and procedures were effective at the reasonable assurance levels.

Management's Report on Internal Control over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting as defined in Rule 13a-15(f) of the Exchange Act. Internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that in reasonable detail accurately and fairly reflect the transactions and dispositions of our assets; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that our receipts and expenditures are being made only in accordance with authorizations of our management and directors; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use or disposition of our assets that could have a material effect on the financial statements.

Under the supervision and with the participation of our management, including our principal executive officer and principal financial officer, we conducted an evaluation of the effectiveness of our internal control over financial reporting based on criteria established in the *Internal Control—Integrated Framework* issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework). Management's assessment included evaluation of such elements as the design and operating effectiveness of key financial reporting controls, process documentation, accounting policies, and our overall control environment. Based on this evaluation, our management concluded that our internal control over financial reporting was effective as of December 31, 2022.

Our management's assessment of the effectiveness of internal control over financial reporting as of December 31, 2022 excluded the internal control over financial reporting at La Jolla and Entasis, which constituted approximately 33% of total assets and 6% of total revenue in our consolidated financial statements as of and for the year ended December 31, 2022. We acquired La Jolla on August 22, 2022 and Entasis on July 11, 2022 and had not completed our evaluation of the internal controls of the acquired businesses as of December 31, 2022. This exclusion was in accordance with Securities and Exchange Commission guidance that an assessment of a recently acquired business may be omitted in management's report on internal controls over financial reporting in the year of acquisition.

Our independent registered public accounting firm, Deloitte & Touche LLP, has audited our internal control over financial reporting as of December 31, 2022. Their attestation report on the audit of our internal control over financial reporting is included below.

Limitations on the Effectiveness of Controls

Our management, including our principal executive officer and principal financial officer, does not expect that our disclosure controls and procedures or our internal control over financial reporting will prevent all errors and all frauds. A control system, no matter how well conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met. Further, the design of a control system must reflect the fact that there are resource constraints, and the benefit of controls must be considered relative to their costs. Because of the inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that all control issues and instances of fraud, if any, within Innoviva have been detected. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

Changes in Internal Control over Financial Reporting

During the year ended December 31, 2022, we completed our acquisitions of Entasis and La Jolla. We are currently in the process of integrating the acquired operations and processes into our internal control environment and implementing necessary changes to our internal control over financial reporting, including, but not limited to, the creation of new controls related to inventory management, research and development activities and product sales.

Other than the above, there have been more material changes to our internal control over financial reporting (as defined in Rule 13a-15(f) of the Exchange Act) for the year ended December 31, 2022 which have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

To the Stockholders and the Board of Directors of Innoviva, Inc.

Opinion on Internal Control over Financial Reporting

We have audited the internal control over financial reporting of Innoviva, Inc. and subsidiaries (the "Company") as of December 31, 2022, based on criteria established in *Internal Control — Integrated Framework (2013)* issued by the Committee of Sponsoring Organizations of the Treadway Commission (COSO). In our opinion, the Company maintained, in all material respects, effective internal control over financial reporting as of December 31, 2022, based on criteria established in *Internal Control — Integrated Framework (2013)* issued by COSO.

We have also audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the consolidated financial statements as of and for the year ended December 31, 2022, of the Company and our report dated February 28, 2023, expressed an unqualified opinion on those financial statements.

As described in Management's Report on Internal Control over Financial Reporting, management excluded from its assessment the internal control over financial reporting at Entasis Therapeutics Holdings Inc. which was acquired on July 11, 2022, and La Jolla Pharmaceutical Company which was acquired on August 22, 2022, and whose financial statements constitute 33% of total assets and 6% of total revenue in the consolidated financial statement amounts as of and for the year ended December 31, 2022. Accordingly, our audit did not include the internal control over financial reporting at Entasis Therapeutics Holdings Inc. and La Jolla Pharmaceutical Company.

Basis for Opinion

The Company's management is responsible for maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting, included in the accompanying Management's Report on Internal Control over Financial Reporting. Our responsibility is to express an opinion on the Company's internal control over financial reporting based on our audit. We are a public accounting firm registered with the PCAOB and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audit in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects. Our audit included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, testing and evaluating the design and operating effectiveness of internal control based on the assessed risk, and performing such other procedures as we considered necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinion.

Definition and Limitations of Internal Control over Financial Reporting

A company's internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

/s/ Deloitte & Touche LLP

San Jose, California
February 28, 2023

ITEM 9B. OTHER INFORMATION

None

ITEM 9C. DISCLOSURE REGARDING FOREIGN JURISDICTIONS THAT PREVENT INSPECTIONS.

Not applicable.

PART III

ITEM 10. DIRECTORS, EXECUTIVE OFFICERS AND CORPORATE GOVERNANCE

The information required by this Item is incorporated by reference from our proxy statement for our 2023 Annual Meeting of Stockholders to be filed with the SEC within 120 days after the end of our fiscal year ended December 31, 2022.

ITEM 11. EXECUTIVE COMPENSATION

The information required by this Item is incorporated by reference from our proxy statement for our 2023 Annual Meeting of Stockholders to be filed with the SEC within 120 days after the end of our fiscal year ended December 31, 2022.

ITEM 12. SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT AND RELATED STOCKHOLDER MATTERS

Other than with respect to the Securities Authorized for Issuance under Equity Compensation Plans below, the information required by this Item is incorporated by reference from our proxy statement for our 2023 Annual Meeting of Stockholders to be filed with the SEC within 120 days after the end of our fiscal year ended December 31, 2022.

Securities Authorized for Issuance under Equity Compensation Plans

The following table provides certain information with respect to all of our equity compensation plans in effect as of December 31, 2022:

Plan Category	Number of securities to be issued upon exercise of outstanding options and vesting of outstanding restricted stock units and restricted stock awards		Weighted-average exercise price of outstanding options		Number of securities remaining available for future issuance under equity compensation plans (excluding securities reflected in column (a))	
	(a)		(b)		(c)	
Equity compensation plans approved by security holders	1,465,720	(1)	15.56	(2)	3,999,265	(3)

(1) Includes 947,906 shares issuable upon exercise of outstanding options and 517,814 shares issuable upon vesting of outstanding RSUs and RSAs.
(2) Does not take into account outstanding restricted stock units as these awards have no exercise price.
(3) Includes 160,995 shares of common stock available under our Employee Stock Purchase Plan.

ITEM 13. CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS, AND DIRECTOR INDEPENDENCE

The information required by this Item is incorporated by reference from our proxy statement for our 2023 Annual Meeting of Stockholders to be filed with the SEC within 120 days after the end of our fiscal year ended December 31, 2022.

ITEM 14. PRINCIPAL ACCOUNTING FEES AND SERVICES

The information required by this Item is incorporated by reference from our proxy statement for our 2023 Annual Meeting of Stockholders to be filed with the SEC within 120 days after the end of our fiscal year ended December 31, 2022.

PART IV

ITEM 15. EXHIBITS AND FINANCIAL STATEMENT SCHEDULES

(a) The following documents are filed as part of this Annual Report on Form 10-K:

1. Financial Statements:

The following financial statements and schedules of the Registrant are contained in Part II, Item 8, "Financial Statements and Supplementary Data" of this Annual Report on Form 10-K:

	Page
Consolidated Balance Sheets as of December 31, 2022 and 2021	86
Consolidated Statements of Income for each of the three years in the period ended December 31, 2022	87
Consolidated Statements of Comprehensive Income for each of the three years in the period ended December 31, 2022	88
Consolidated Statements of Stockholders' Equity for each of the three years in the period ended December 31, 2022	89
Consolidated Statements of Cash Flows for each of the three years in the period ended December 31, 2022	90
Notes to Consolidated Financial Statements	92
Reports of Independent Registered Public Accounting Firm (PCAOB ID 34)	131
Report of Independent Registered Public Accounting Firm (PCAOB ID 248)	133

2. Financial Statement Schedules:

All schedules have been omitted because of the absence of conditions under which they are required or because the required information, where material, is shown in the financial statements, financial notes or supplementary financial information.

(b) Exhibits required by Item 601 of Regulation S-K:

The information required by this Item is set forth on the exhibit index that follows the signature page of this report.

ITEM 16. FORM 10-K SUMMARY

None.

Exhibits

Exhibit Number	Description	Incorporated by Reference			Filed Herewith
		Form	Exhibit	Filing Date/Period End Date	
2.1	Agreement and Plan of Merger, dated as of May 23, 2022, by and among Innoviva, Inc., Innoviva Merger Sub, Inc. and Entasis Therapeutics	8-K	2.1	5/24/2022	
2.2	Agreement and Plan of Merger, dated as of July 10, 2022, by and among Innoviva, Inc., Innoviva Acquisition Sub, Inc. and La Jolla Pharmaceutical Company	8-K	2.1	7/11/2022	
3.1	Amended and Restated Certificate of Incorporation	S-1	3.3	7/26/2004	
3.2	Certificate of Amendment of Restated Certificate of Incorporation	10-Q	3.4	3/31/2007	
3.3	Certificate of Ownership and Merger Merging LABA Merger Sub, Inc. with and into Theravance, Inc., as filed with the Secretary of State of the State of Delaware, effective on January 7, 2016	8-K	3.1	1/8/2016	
3.4	Amended and Restated Bylaws, amended and restated as of February 8, 2017	8-K	3.1	2/9/2017	
4.1	Specimen certificate representing the common stock of the registrant	10-K	4.1	12/31/2006	
4.2	Indenture, dated as of January 24, 2013 by and between Theravance, Inc. and The Bank of New York Mellon Trust Company, N.A., as trustee	8-K	4.1	1/25/2013	
4.3	Form of 2.125% Convertible Subordinated Note Due 2023 (included in Exhibit 4.4)				
4.4	Indenture (including form of Note) with respect to Innoviva's 2.50% Convertible Senior Notes due 2025, dated as of August 7, 2017, between Innoviva and The Bank of New York Mellon Trust Company, N.A., as trustee	8-K	4.1	8/7/2017	
4.5	Description of Registrant's Securities Registered Pursuant to Section 12 of the Securities Exchange Act of 1934	10-K	4.9	2/19/2020	
4.6	Indenture (including form of Note) with respect to Innoviva's 2.125% Convertible Senior Notes due 2028, dated as of March 7, 2022, between Innoviva, Inc. and The Bank of New York Mellon Trust Company, N.A., as trustee	8-K	4.1	3/8/2022	
10.1	Employee Stock Purchase Plan, as amended April 27, 2010	10-Q	10.4	6/30/2010	
10.2	Collaboration Agreement between the registrant and Glaxo Group Limited, dated as of November 14, 2002	10-Q	10.1	6/30/2014	
10.3	Amended and Restated Investors' Rights Agreement by and among the registrant and the parties listed therein, dated as of May 11, 2004	S-1	10.13	6/10/2004	
10.4*	Strategic Alliance Agreement between the registrant and Glaxo Group Limited, dated as of March 30, 2004	10-K	10.13	12/31/2013	
10.5+	Description of Cash Bonus Program, as amended	10-K	10.22	12/31/2009	
10.6+	Amendment to Change in Control Severance Plan effective December 16, 2009	10-K	10.47	12/31/2009	
10.7+	2009 Change in Control Severance Plan adopted December 16, 2009	10-K	10.48	12/31/2009	
10.8	Second Amendment to Amended and Restated Governance Agreement among the registrant, Glaxo Group Limited, GlaxoSmithKline plc and GlaxoSmithKline LLC, dated as of November 29, 2010	8-K	10.2	11/29/2010	
10.9	Amendment to Strategic Alliance Agreement, dated October 3, 2011	10-K	10.34	12/31/2011	
10.10+	2012 Equity Incentive Plan, as approved by the board of directors February 8, 2012 and approved by stockholders May 16, 2012 and forms of equity award	10-Q	10.38	6/30/2012	
10.11	Base Capped Call Transaction, dated January 17, 2013	8-K	10.1	1/23/2013	
10.12	Additional Capped Call Transaction, dated January 18, 2013	8-K	10.2	1/23/2013	
10.13	Master Agreement by and among Theravance, Inc., Theravance Biopharma, Inc. and Glaxo Group Limited, dated March 3, 2014	8-K/A	10.1	3/6/2014	
10.14*	Collaboration Agreement Amendment by and between Theravance, Inc. and Glaxo Group Limited, dated March 3, 2014	8-K/A	10.2	3/6/2014	
10.15*	Strategic Alliance Agreement Amendment by and between Theravance, Inc. and Glaxo Group Limited, dated March 3, 2014	8-K/A	10.3	3/6/2014	

10.16	Transition Services Agreement between Theravance and Theravance Biopharma, dated June 2, 2014	8-K	10.2	6/5/2014	
10.17	Tax Matters Agreement between Theravance and Theravance Biopharma, dated June 2, 2014	8-K	10.3	6/5/2014	
10.18	Employee Matters Agreement between Theravance and Theravance Biopharma, dated June 1, 2014	8-K	10.4	6/5/2014	
10.19	Theravance Respiratory Company, LLC Limited Liability Company Agreement between Theravance and Theravance Biopharma, dated May 31, 2014	8-K	10.5	6/5/2014	
10.20	Amendment/Clarification to Transition Services Agreement between Theravance and Theravance Biopharma, dated March 2, 2015	10-Q	10.64	3/31/2015	
10.21+	First Amendment to 2009 Change In Control Severance Plan (Renamed 2009 Severance Plan)	8-K	10.2	7/29/2015	
10.22	Form of Notice of Performance-Based Restricted Stock Award and Restricted Stock Award Agreement under 2012 Equity Incentive Plan (director form)	10-K	10.76	2/23/2018	
10.23+	Second Amendment to 2009 Severance Plan	10-Q	10.81	7/26/2018	
10.24+	Offer Letter with Marianne Zhen, dated September 7, 2018	8-K	10.1	9/11/2018	
10.25+	Offer Letter between Innoviva, Inc. and Pavel Raifeld, dated May 20, 2020	8-K	10.1	5/26/2020	
10.26+	Offer Letter between Innoviva, Inc. and Pavel Raifeld, dated April 29, 2022	8-K	10.1	5/2/2022	
10.27	Strategic Advisory Agreement, dated as of December 11, 2020, by and between Sarissa Capital Management LP and Innoviva, Inc.	8-K	10.1	12/14/2020	
10.28	Amended and Restated Limited Partnership Agreement of ISP Fund LP, dated as of December 11, 2020, by and among ISP Fund LP, Sarissa Capital Fund GP LP, Innoviva Strategic Partners LLC and the other parties named therein	8-K	10.2	12/14/2020	
10.29	Share Repurchase Agreement, dated as of May 2021, by and between Innoviva, Inc. and Glaxo Group Limited	8-K	10.1	5/20/2021	
10.30	Letter Agreement, dated as of May 20, 2021, by and among Innoviva Strategic Partners LLC, ISP Fund LP and Sarissa Capital Fung GP LP	8-K	10.2	5/20/2021	
10.31	Capped Call Confirmation dated March 2, 2022, by and among Innoviva, Inc., Bank of America, N.A., Goldman Sachs & Co. LLC and Deutsche Bank AG, London Branch	8-K	10.1	3/8/2022	
10.32	Amendment No. 1 to the Investor Rights Agreement, dated May 23, 2022, by and among Innoviva, Inc. and Entasis Therapeutics Holdings Inc.	8-K	10.1	5/24/2022	
10.33	Support Agreement, dated July 10, 2022, by and among Innoviva, Inc., Innoviva Acquisition Sub, Inc., Tang Capital Partners, LP and Kevin C. Tang Foundation	8-K	10.1	7/11/2022	
10.34	Equity Purchase Agreement, dated July 13, 2022, by and among Innoviva, Inc., Innoviva TRC Holdings LLC and Royalty Pharma Investments 2019 ICAV	8-K	10.1	7/13/2022	
10.35	Third Amendment to Collaboration Agreement, dated July 13, 2022, by and among Innoviva, Inc., Glaxo Group Limited, and Theravance Respiratory Company, LLC.	8-K	10.2	7/13/2022	
21.1	List of Subsidiaries				X
23.1	Consent of Independent Registered Public Accounting Firm				X
23.2	Consent of Independent Registered Public Accounting Firm				X
23.3	Consent of Ernst & Young LLP Independent Registered Public Accounting Firm of Armata Pharmaceuticals, Inc.**				
24.1	Power of Attorney (see signature page to this Annual Report on Form 10-K)				X
31.1	Certification of Principal Executive Officer Pursuant to Rule 13a-14 under the Securities Exchange Act of 1934				X
31.2	Certification of Principal Financial Officer Pursuant to Rule 13a-14 under the Securities Exchange Act of 1934				X
32#	Certifications Pursuant to 18 U.S.C. Section 1350				

99.1	Audited Consolidated Financial Statements of Armata Pharmaceuticals, Inc. at December 31, 2022, for the year ended December 31, 2022**	
101.INS	Inline XBRL Instance Document - the instance document does not appear in the Interactive Data File because its XBRL tags are embedded within the Inline XBRL document.	X
101.SCH	Inline XBRL Taxonomy Extension Schema Document	X
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document	X
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document	X
101.LAB	Inline XBRL Taxonomy Extension Label Linkbase Document	X
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document	X
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)	X

+ Management contract or compensatory plan or arrangement required to be filed pursuant to Item 15(b) of Form 10-K.

* Confidential treatment has been granted for certain portions which are omitted in the copy of the exhibit electronically filed with the Securities and Exchange Commission. The omitted information has been filed separately with the Securities and Exchange Commission pursuant to Innoviva, Inc.'s application for confidential treatment.

** To be filed by amendment to this Annual Report on Form 10-K.

Furnished herewith.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the Registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

INNOVIVA, INC.

Date: February 28, 2023

By: /s/ PAVEL RAIFELD
Pavel Raifeld
Chief Executive Officer

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Pavel Raifeld, as their true and lawful attorney-in-fact and agent, with full power of substitution and resubstitution, for such person and in his or her name, place and stead, in any and all capacities, to sign any and all amendments to the Annual Report on Form 10-K, and to file the same, with all exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorney-in-fact and agent full power and authority to do and perform each and every act and thing requisite and necessary to be done in and about the premises, as fully to all intents and purposes as he or she could do in person, hereby ratifying and confirming all that said attorney-in-fact and agent, or his substitutes, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following persons on behalf of the registrant and in the capacities and on the dates indicated.

Signature	Title	Date
/s/ PAVEL RAIFELD Pavel Raifeld	Chief Executive Officer (Principal Executive Officer)	February 28, 2023
/s/ MARIANNE ZHEN Marianne Zhen	Chief Accounting Officer (Principal Financial Officer)	February 28, 2023
/s/ GEORGE BICKERSTAFF George Bickerstaff, III	Chairman of the Board	February 28, 2023
/s/ ODYSSEAS KOSTAS Odysseas Kostas, M.D.	Director	February 28, 2023
/s/ MARK DIPAOLO Mark DiPaolo, Esq.	Director	February 28, 2023
/s/ JULES HAIMOVITZ Jules Haimovitz.	Director	February 28, 2023
/s/ SARAH SCHLESINGER Sarah Schlesinger, M.D.	Director	February 28, 2023
/s/ DEBORAH L. BIRX Deborah L. Birx, M.D.	Director	February 28, 2023
/s/ SAPNA SRIVASTAVA Sapna Srivastava, Ph.D.	Director	February 28, 2023

Exhibit 21.1

LIST OF SUBSIDIARIES

Name	Jurisdiction	Ownership Interest
Advanced Medicine East, Inc	Delaware	100%
Innoviva Strategic Partners LLC	Delaware	100%
Innoviva Royalty Sub LLC	Delaware	100%
Innoviva TRC Holdings LLC	Delaware	100%
Innoviva Strategic Opportunities LLC	Delaware	100%
ISP Fund LLP	Delaware	100%
Innoviva Specialty Therapeutics Holdings LLC	Delaware	100%
Innoviva Specialty Therapeutics Inc.	Delaware	100%
Entasis Therapeutics Holdings Inc.	Delaware	100%
Entasis Therapeutics Inc.	Delaware	100%
Entasis Therapeutics Limited	United Kingdom	100%
Entasis Therapeutics Security Corporation	Massachusetts	100%
Entasis Therapeutics (Ireland) Limited	Ireland	100%
La Jolla Pharmaceutical Company	Delaware	100%
La Jolla Pharma, LLC	Delaware	100%
Tetraphase Pharmaceuticals, Inc.	Delaware	100%
La Jolla Pharmaceutical Holdings, LLC	Delaware	100%
La Jolla Pharmaceutical I B.V.	Netherlands	100%
La Jolla Pharmaceutical II B.V.	Netherlands	100%
La Jolla Pharmaceutical III B.V.	Netherlands	100%

Exhibit 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We consent to the incorporation by reference in Registration Statement Nos. 333-119559, 333-129669, 333-150753, 333-159042, 333-173923, 333-181763, and 333-197950 on Form S-8 of our reports dated February 28, 2023, relating to the financial statements of Innoviva, Inc. and the effectiveness of Innoviva, Inc.'s internal control over financial reporting appearing in this Annual Report on Form 10-K for the year ended December 31, 2022.

/s/ Deloitte & Touche LLP

San Jose, California
February 28, 2023

Exhibit 23.2

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We have issued our report dated February 28, 2022, with respect to the consolidated financial statements included in the Annual Report of Innoviva, Inc. on Form 10-K for the year ended December 31, 2022. We consent to the incorporation by reference of said report in the Registration Statements of Innoviva, Inc. on Forms S-8 (File No. 333-119559, File No. 333-129669, File No. 333-150753, File No. 333-159042, File No. 333-173923, File No. 333-181763, and File No. 333-197950).

/s/ GRANT THORNTON LLP

San Francisco, California
February 28, 2023

Exhibit 31.1

Certification of Principal Executive Officer
Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002

I, Pavel Raifeld, certify that:

1. I have reviewed this Annual Report on Form 10-K of Innoviva, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15(d)-15(f)) for the registrant and have:

   a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: February 28, 2023

/s/ PAVEL RAIFELD
Pavel Raifeld
Chief Executive Officer
(Principal Executive Officer)

Exhibit 31.2

Certification of Principal Accounting Officer
Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002

I, Marianne Zhen, certify that:

1. I have reviewed this Annual Report on Form 10-K of Innoviva, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15(d)-15(f)) for the registrant and have:

   a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: February 28, 2023

/s/ MARIANNE ZHEN

Marianne Zhen
Chief Accounting Officer
(Principal Financial Officer)

Exhibit 32

CERTIFICATIONS OF PRINCIPAL EXECUTIVE OFFICER
AND PRINCIPAL ACCOUNTING OFFICER
PURSUANT TO
18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

I, Pavel Raifeld, certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that the Annual Report of Innoviva, Inc. on Form 10-K for the fiscal year ended December 31, 2022 fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended and that information contained in such Annual Report on Form 10-K fairly presents in all material respects the financial condition of Innoviva, Inc. at the end of the periods covered by such Annual Report on Form 10-K and results of operations of Innoviva, Inc. for the periods covered by such Annual Report on Form 10-K.

Date: February 28, 2023

By: /s/ PAVEL RAIFELD
Pavel Raifeld
Chief Executive Officer
(Principal Executive Officer)

I, Marianne Zhen, certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that the Annual Report of Innoviva, Inc. on Form 10-K for the fiscal year ended December 31, 2022 fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934, as amended and that information contained in such Annual Report on Form 10-K fairly presents in all material respects the financial condition of Innoviva, Inc. at the end of the periods covered by such Annual Report on Form 10-K and results of operations of Innoviva, Inc. for the periods covered by such Annual Report on Form 10-K.

Date: February 28, 2023

By: /s/ MARIANNE ZHEN
Marianne Zhen
Chief Accounting Officer
(Principal Financial Officer)

A signed original of this written statement required by Section 906 has been provided to Innoviva, Inc. and will be retained by it and furnished to the Securities and Exchange Commission or its staff upon request.