UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, DC 20549

FORM 8-K

Current Report Pursuant
to Section 13 or 15(d) of the
Securities Exchange Act of 1934

Date of Report (Date of earliest event Reported): **May 9, 2013**

THERAVANCE, INC.

(Exact Name of Registrant as Specified in its Charter)

Delaware	**000-30319**	**94-3265960**
(State or Other Jurisdiction of Incorporation)	(Commission File Number)	(I.R.S. Employer Identification Number)

901 Gateway Boulevard
South San Francisco, California 94080
(650) 808-6000
(Addresses, including zip code, and telephone numbers, including area code, of principal executive offices)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (see General Instruction A.2. below):

o Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

o Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

o Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

o Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Item 7.01 Regulation FD Disclosure.

The information in this Current Report (including Exhibits 99.1, 99.2 and 99.3) is being furnished and shall not be deemed "filed" for the purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Securities Exchange Act of 1934"), or otherwise subject to the liabilities of that Section. The information in this Current Report (including Exhibits 99.1, 99.2 and 99.3) shall not be incorporated by reference into any registration statement or other document pursuant to the Securities Act of 1933, as amended, except as shall be expressly set forth by specific reference in such filing.

On May 9, 2013 at the 32nd Annual Scientific Meeting of the American Pain Society, New Orleans, Louisiana, posters presenting information from Theravance, Inc.'s Study 76 and Study 84 of the Phase 2b program with TD-1211 in patients with opioid-induced constipation were made available for viewing. TD-1211 is an investigational once-daily, orally administered, peripherally selective, multivalent inhibitor of the mu opioid receptor designed with a goal of alleviating gastrointestinal side effects of opioid therapy without affecting analgesia. Copies of the posters are furnished as Exhibits 99.1, 99.2 and 99.3 to this report and are incorporated herein by reference.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits.

Exhibit	Description
Exhibit 99.1	TD-1211 Demonstrates Tolerability and Clinical Activity Following Multiple Treatment Administration Strategies in Patients with Opioid-Induced Constipation

Exhibit 99.2	TD-1211 Demonstrates a Durable Increase in Bowel Movement Frequency and Return Toward Normal Bowel Function in a 5-Week Phase 2b Opioid-Induced Constipation Study
Exhibit 99.3	No Evidence of Analgesic Interference or CNS Opioid Withdrawal for TD-1211 in a Phase 2b Study in Opioid-Induced Constipation

SIGNATURE

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

THERAVANCE, INC.

Date: May 9, 2013

By: /s/ Michael W. Aguiar
Michael W. Aguiar
Chief Financial Officer

EXHIBIT INDEX

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Exhibit 99.1

Poster 376
APS2013, New Orleans, LA
rvickery@theravance.com

TD-1211 Demonstrates Tolerability and Clinical Activity Following Multiple Treatment Administration Strategies in Patients with Opioid-Induced Constipation

Neil Singla(1), Daniel Canafax(2), Angela Kang(2), Yu-Ping Li(2), Ullrich Schwertschlag(2), Lynn Webster(3), and Ross Vickery(2)

(1) Lotus Clinical Research, Inc., Pasadena, CA; (2) Theravance, Inc., South San Francisco, CA; (3) Lifetree Clinical Research, Inc., Salt Lake City, UT

Introduction

- Opioid analgesics such as morphine continue to play a critical role in chronic cancer and non-cancer pain control.(1) Despite their effectiveness, opioids have significant drawbacks, notably the development of analgesic tolerance and physical dependence, sedation, respiratory depression and bowel dysfunction.(2)
- Opioid-induced constipation (OIC) is common, affecting up to 80% of patients receiving opioids for chronic non-cancer pain.(3)
- TD-1211 is an investigational, peripherally selective, mu-opioid receptor antagonist designed to alleviate gastrointestinal side effects of opioid therapy without affecting analgesia.
- TD-1211 was assessed in a Phase 2, single-blind exploratory study in 95 adult patients with OIC.
- The safety and tolerability of various doses, dosing strategies and dose escalations of TD-1211, as well as efficacy results, from this study are reported here.

Methods

- A single-blind, multi-center, six-cohort study was conducted in chronic non-cancer pain patients with OIC, defined as $\leq$5 spontaneous bowel movements (SBMs) over a 2-week baseline period and at least one additional symptom of constipation in at least 25% of the bowel movements.
- The first four cohorts received an oral dose of TD-1211 5mg once daily for either 4 days (Cohorts 1 and 2) or 2 days (Cohorts 3 and 4), followed by an increase in daily dose to either 10mg or 15mg for two weeks. Cohort 5 received 2mg once daily and cohort 6 received 2.5mg q6h for two weeks without dose escalation (**Figure 1**).
- For at least 14 days prior to Day 1, patients were on a stable chronic opioid regimen, with a total daily dose of $\geq$30mg morphine equivalent units (MEU).
- Patients were required to stop laxatives and bowel regimens, except protocol-permitted rescue bisacodyl use, throughout the study.
- Electronic diaries collected frequency, timing, and symptoms of bowel movements; use of laxatives and opioids; and daily pain scores.
- The primary study objective was to evaluate the safety and tolerability of TD-1211 5mg once daily as an initiation dose, for 4 or 2 days, escalated to 10mg or 15mg once daily as maintenance therapy for 2 weeks.
- Additional study objectives were to examine the tolerability and effects of a TD-1211 2mg qd dose and a TD-1211 2.5mg q6h dose administered for two weeks; and to assess the efficacy of TD-1211 10mg and 15mg doses.

Results

Patient baseline characteristics

- 95 patients were enrolled, 16 patients per cohort, except Cohort 6 which enrolled 15 patients.
- 12 (12.6%) patients terminated study early; 6 due to adverse events (AEs); 2 each for physician decision and withdrawal by subject; and 1 each for other and protocol deviation.

Demographics

- Mean age was 48.0 years (range = 22.0 to 65.0) and was similar across cohorts.
- 55.8% of patients were female and 78.9% were white.

OIC

- Mean baseline daily oral opioid dose ranged across cohorts from 93 to 170 MEU, with the lowest and highest doses being 30 and 745 MEU, respectively.
- During the baseline period, 55% of patients used bisacodyl, and bisacodyl was not used more than 3 days by any patient.
- Mean baseline SBMs/week was 0.9 to 1.7; mean baseline complete spontaneous bowel movements (CSBMs)/week was 0.1 to 0.6.

Figure 1: Study Schematic

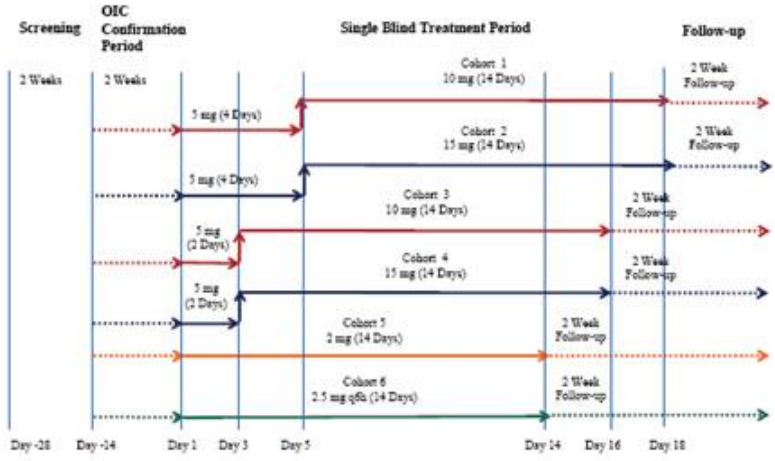


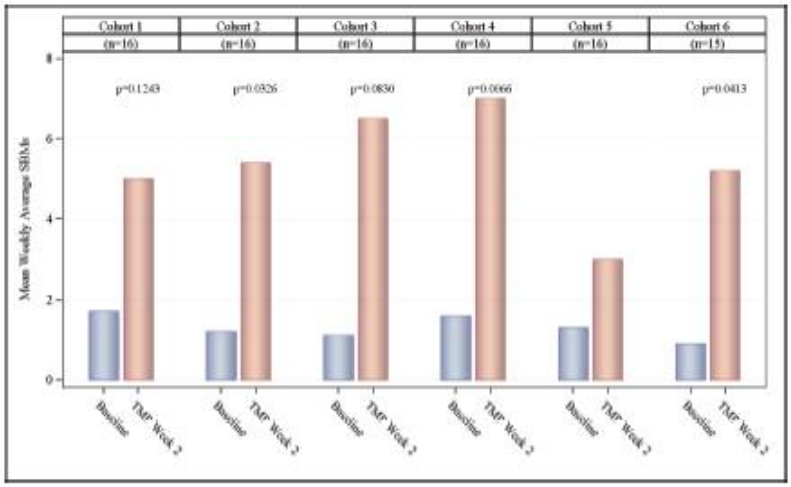
Table 1: Adverse Events Reported in ≥ 5% of Patients

	TD-1211						
Safety Population	**Cohort 1 (n=16)**	**Cohort 2 (n=16)**	**Cohort 3 (n=16)**	**Cohort 4 (n=16)**	**Cohort 5 (n=16)**	**Cohort 6 (n=15)**	**All TD-1211 (N=95)**
Any AEs, n (%)	7 (43.8)	11 (68.8)	9 (56.3)	8 (50.0)	3 (18.8)	6 (40.0)	44 (46.3)
Gastrointestinal Disorders	5 (31.3)	7 (43.8)	6 (37.5)	4 (25.0)	3 (18.8)	6 (40.0)	31 (32.6)
Abdominal Distension	2 (12.5)	1 (6.3)	0	1 (6.3)	0	1 (6.7)	5 (5.3)
Abdominal Pain	1 (6.3)	1 (6.3)	3 (18.8)	3 (18.8)	2 (12.5)	4 (26.7)	14 (14.7)
Diarrhea	0	2 (12.5)	3 (18.8)	0	1 (6.3)	0	6 (6.3)
Flatulence	0	2 (12.5)	2 (12.5)	1 (6.3)	0	3 (20.0)	8 (8.4)
Nausea	1 (6.3)	3 (18.8)	3 (18.8)	1 (6.3)	0	1 (6.7)	9 (9.5)
Nervous System Disorders	2 (12.5)	2 (12.5)	4 (25.0)	0	0	1 (6.7)	9 (9.5)
Headache	2 (12.5)	2 (12.5)	2 (12.5)	0	0	0	6 (6.3)

Table 2: GI-Related Adverse Events; 4-Day and 2-Day Initiation Periods

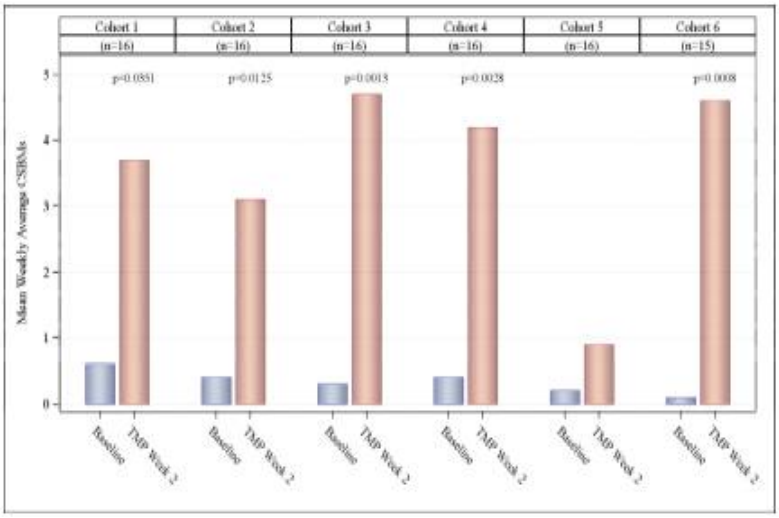
	TD-1211					
Safety Population	**Cohort 1 (n=16)**	**Cohort 2 (n=16)**	**Combined 1 & 2 (n=32)**	**Cohort 3 (n=16)**	**Cohort 4 (n=16)**	**Combined 3 & 4 (n=32)**
	4-Day Initiation Period			**2-Day Initiation Period**		
Any GI-related AEs of interest, n (%)	1 (6.3)	2 (12.5)	3 (9.4)	3 (18.8)	3 (18.8)	6 (18.8)
Abdominal Pain	0	1 (6.3)	1 (3.1)	3 (18.8)	3 (18.8)	6 (18.8)
Diarrhea	0	0	0	2 (12.5)	0	2 (3.1)
Nausea	1 (6.3)	1 (6.3)	2 (6.3)	2 (12.5)	1 (6.3)	3 (9.4)
Vomiting	0	0	0	1 (6.3)	0	1 (3.1)

Figure 2: Spontaneous Bowel Movements



Intent to Treat Population (ITT) - observed cases TMP = treatment maintenance period.

Figure 3: Complete Spontaneous Bowel Movements



Intent to Treat Population (ITT) - observed cases. TMP = treatment maintenance period.

Primary study objective

· TD-1211 was generally well tolerated at all dose levels tested (**Table 1**) .
· Initiating treatment with TD-1211 5mg for 4 days resulted in fewer GI-related AEs (**Table 2**).
· Escalating TD-1211 to 10mg versus 15mg did not produce unexpected AEs or events of greater severity **(Table 1).**

Secondary tolerability and safety objectives

· The majority of treatment-related GI AEs were associated with initiation of treatment, resolved within a few days, and were mild or moderate in severity.
· No treatment-emergent serious adverse events (SAEs) were reported.
· There were no reports of central opioid withdrawal.
· No clinically significant laboratory, ECG, or vital sign abnormalities were observed.

Efficacy

· Study 0076 was not powered to show statistical differences between the various doses of TD-1211.
· TD-1211 10mg and 15mg mean change from baseline at Week 2 in SBM frequency ranged from 3.3 to 5.4.
· TD-1211 10mg and 15mg mean change from baseline at Week 2 in CSBM frequency ranged from 2.8 to 4.4.
· TD-1211 2mg demonstrated minimal activity with a mean increase from baseline at Week 2 of 1.8 SBMs and 0.7 CSBMs
· TD-1211 2.5mg q6h was clinically active with a mean increase from baseline at Week 2 of 4.3 SBMs and 4.5 CSBMs.

TD-1211 Conclusions

· TD-1211 was generally well-tolerated at dose levels up to 15mg. Majority of GI AEs resolved within a few days, and all GI AEs resolved without sequelae.
· There were no treatment-emergent SAEs.
· Initiation of dosing at 5mg before escalating to 10mg or 15mg resulted in fewer GI-related AEs.
· No evidence of centrally-mediated opioid withdrawal.
· TD-1211 10mg and 15mg administered orally once a day demonstrated a clinically meaningful response at Week 2.
· These results support further development of a 5mg treatment initiation dose followed by maintenance therapy at up to 15mg qd.

References

(1) Walsh, T.D. (2000). Seminars in Oncology, 27, 45-63.
(2) Walsh, T.D. (1990). J. Pain Symptom Manage., 5, 362-367.
(3) Holzer, P. (2012). Current Pharmaceutical Design, 18, 6010-6020.

Exhibit 99.2

Poster 411
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TD-1211 Demonstrates a Durable Increase in Bowel Movement Frequency and Return Toward Normal Bowel Function in a 5-Week Phase 2b Opioid-Induced Constipation Study

Ross Vickery(1), Yu-Ping Li(1), Ullrich Schwertschlag(1), Neil Singla(2), Lynn Webster(3), and Daniel Canafax(1)

(1) Theravance, Inc., South San Francisco, CA; (2) Lotus Clinical Research, Inc., Pasadena, CA; (3) CRI Lifetree, Inc., Salt Lake City, UT

Introduction

- Opioid analgesics such as morphine continue to play a critical role in chronic cancer and non-cancer pain control.(1) Despite their effectiveness, opioids have significant drawbacks, notably the development of analgesic tolerance and physical dependence, sedation, respiratory depression and bowel dysfunction.(2)
- Opioid-induced constipation (OIC) is common, affecting up to 80% of patients receiving opioids for chronic non-cancer pain.(3)
- TD-1211 is an investigational, peripherally selective, mu-opioid receptor antagonist designed to alleviate gastrointestinal side effects of opioid therapy without affecting analgesia.
- Safety and efficacy results, including the primary and key secondary endpoints, from a 5-week, Phase 2b study in chronic non-cancer pain OIC patients have been previously reported (see also **APS 2013 Poster #421**).(4)
- As mu-opioid receptor antagonists can quickly reverse the effects of opioid agonists on gastrointestinal opioid receptors, demonstration of a sustained response on bowel movement frequency is necessary for a therapy intended for patients taking opioids chronically.
- Therefore, additional pre-specified week-by-week efficacy analyses are reported here.

Methods

- A 5-week, double-blind, randomized, multi-center, placebo-controlled, parallel-group study was conducted in chronic non-cancer pain patients with OIC, defined as ≤5 spontaneous bowel movements (SBMs) over a 2-week baseline period and at least one additional symptom of constipation in at least 25% of the bowel movements.
- For the first 4 days of dosing, patients randomized to TD-1211 received 5mg daily and on Day 5, remained at 5mg or were dose-escalated to 10mg or 15mg daily for the remainder of the treatment period. Patients randomized to placebo received placebo for all 5 weeks.
- For at least 14 days prior to Day 1, patients were on a stable chronic opioid regimen, with a total daily dose of ≥30mg morphine equivalent units (MEU).
- Patients were required to stop laxatives and bowel regimens, except protocol-permitted rescue bisacodyl use, throughout the study.
- Electronic diaries collected frequency, timing, and symptoms of bowel movements; use of laxatives and opioids; daily pain scores; and satisfaction / quality of life metrics.
- Week 1 was excluded from the primary analysis in order to confirm the durability of response and predictability of longer term efficacy studies.

Results

Patient baseline demographics

- As shown in **Table 1**, baseline characteristics were similar for all treatment groups.
- Subjects were on a representative spectrum of opioids.
- Daily opioid doses ranged from 30-1740 oral MEU.
- Back pain was the most commonly reported reason for chronic opioid use.

Table 1: Patient Baseline Demographics

		TD-1211		
Modified Intent to Treat Population	**Placebo (N=54)**	**5 mg (N=55)**	**10 mg (N=53)**	**15 mg (N=53)**
Mean Age (years)	47.6	48.3	49.2	48.9
Female Gender	28	37	32	30
BMI Mean (kg/m^2)	28.3	27.8	27.8	28.1
Duration of OIC Mean (years)	5.5	6.4	6.7	5.3

Durability of Response

- An increase in complete spontaneous bowel movements (CSBMs) was observed in Week 1 vs. baseline for each treatment group (**Figure 1**). The increased CSBMs per week was sustained for each week during Weeks 2-5, ranging from between 2.5 to 3.3 for 10mg TD-1211 patients, 2.5 to 2.9 for 15mg TD-1211 patients, and 0.9 to 1.2 for placebo patients.
- Similarly, an increase in SBMs was observed in Week 1 vs. baseline for each treatment group (**Figure 2**). The increased SBMs per week was sustained for each week during Weeks 2-5, ranging from between 4.1 to 4.9 for 10mg TD-1211 patients, 4.6 to 5.2 for 15mg TD-1211 patients, and 2.6 to 3.3 for placebo patients.
- In an exploratory analysis, the mean number of days per week with at least 1 SBM ranged weekly between 3.3 to 3.8 for 10mg TD-1211 patients, 3.6 to 3.9 for 15mg TD-1211 patients, and 2.4 to 2.8 for placebo patients. (**Figure 3**)
- During Weeks 2-5 of treatment, 51-53% of 15mg TD-1211 patients reported ≥5 SBMs per week compared to 14-29% of placebo patients, indicating a return toward normal bowel function for treated patients. (**Figure 4**)

Tolerability and Safety

- TD-1211 was generally well tolerated, with overall treatment emergent adverse events (TEAEs) similar between TD-1211 and placebo and gastrointestinal (GI) TEAEs predominant.

· The majority of treatment-related GI AEs were associated with initiation of treatment, resolved within a few days, and were mild or moderate.

Figure 1: Mean Number of Complete and Spontaneous Bowel Movements (CSBMs) at Each Week

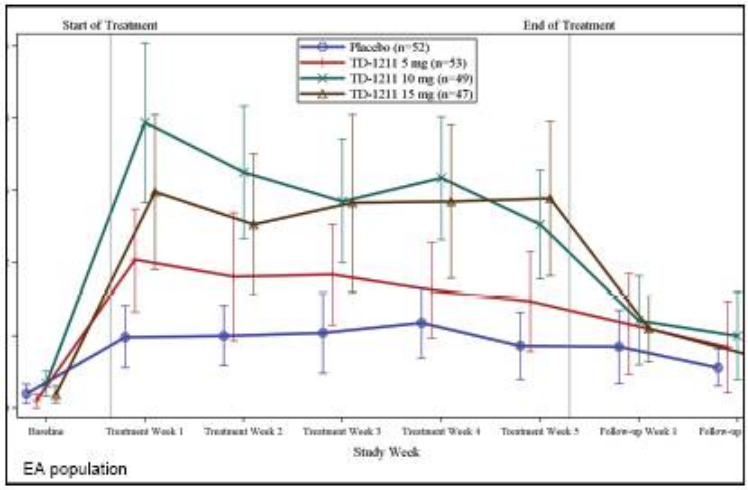

Figure 2: Mean Number of Spontaneous Bowel Movements (SBMs) at Each Week

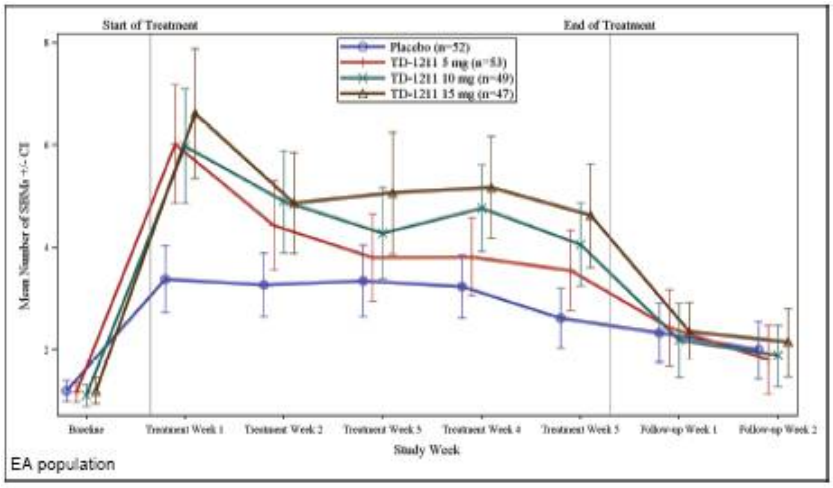

Figure 3: Mean Number of Days per Week with at Least 1 SBM

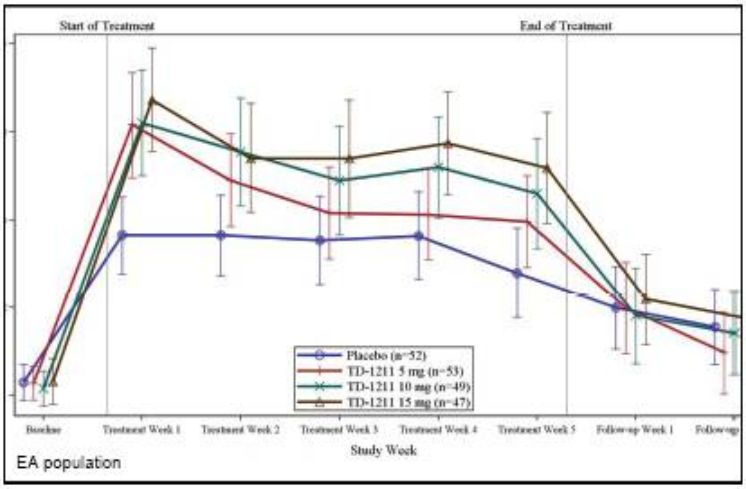

Figure 4: Percent of Patients Reporting ≥5 SBMs per Week on Treatment

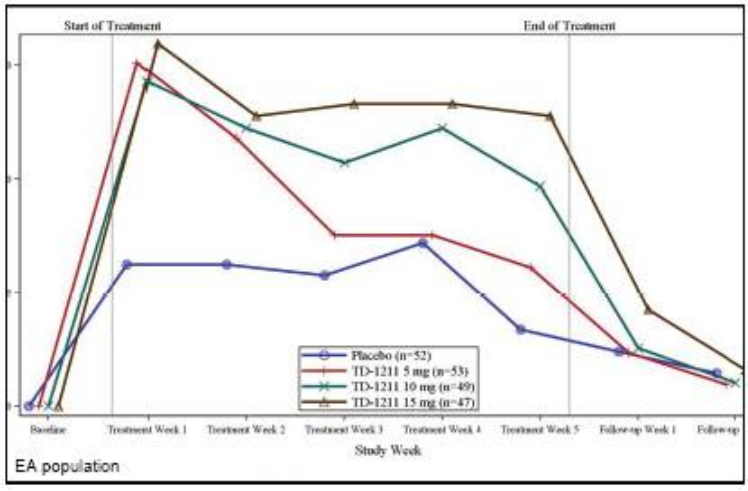

Table 2: GI-Related Adverse Events Occurring After the Dose Initiation Period (≥ Day 5)

		TD-1211 Randomization Group			
	Placebo (n=54)	**5 mg (n=56)**	**10 mg (n=53)**	**15 mg (n=52)**	**All (n=161)**
Any GI-related TEAE of interest	3 (5.6%)	7 (12.5%)	10 (18.9%)	3 (5.8%)	20 (12.4%)
Abdominal pain	1 (1.9%)	3 (5.4%)	4 (7.5%)	1 (1.9%)	8 (5.0%)
Mild	1 (1.9%)	0	3 (5.7%)	0	3 (1.9%)
Moderate	0	3 (5.4%)	1 (1.9%)	1 (1.9%)	5 (3.1%)
Severe	0	0	0	0	0
Abdominal cramping	1 (1.9%)	1 (1.8%)	3 (5.7%)	0	4 (2.5%)
Mild	1 (1.9%)	0	2 (3.8%)	0	2 (1.2%)
Moderate	0	1 (1.8%)	1 (1.9%)	0	2 (1.2%)
Severe	0	0	0	0	0
Diarrhea	0	4 (7.1%)	5 (9.4%)	2 (3.8%)	11 (6.8%)
Mild	0	0	3 (5.7%)	2 (3.8%)	5 (3.1%)
Moderate	0	3 (5.4%)	2 (3.8%)	0	5 (3.1%)
Severe	0	1 (1.8%)	0	0	1 (0.6%)
Nausea	1 (1.9%)	2 (3.6%)	6 (11.3)	1 (1.9%)	9 (5.6%)
Mild	1 (1.9%)	0	5 (9.4%)	1 (1.9%)	6 (3.7%)
Moderate	0	2 (3.6%)	1 (1.9%)	0	3 (1.9%)
Severe	0	0	0	0	0
Vomiting	1 (1.9%)	2 (3.6%)	0	0	2 (1.2%)
Mild	0	0	0	0	0
Moderate	1 (1.9%)	1 (1.8%)	0	0	1 (0.6%)
Severe	0	1 (1.8%)	0	0	1 (0.6%)

Tolerability and Safety (con't)

- At target doses (i.e., after the first 4 days of treatment initiation at 5mg for patients randomized to TD-1211), <13% of all patients reported any GI-related TEAE (**Table 2**). Two severe AEs (diarrhea and vomiting) were noted.
- No treatment-related serious adverse events (SAEs) were reported.
- No clinically significant laboratory, ECG, or vital sign abnormalities were observed.

TD-1211 Conclusions

- 10mg and 15mg demonstrated a clinically meaningful, sustained response in CSBM and SBM frequency over the duration of the treatment period in OIC patients.
- CSBM and SBM frequency measures indicated a return toward normal bowel function for the 2 highest doses.
- Generally well-tolerated with no treatment-related SAEs.
- Majority of treatment-related GI AEs were associated with initiation of treatment, resolved within a few days, and were mild or moderate.

References

(1) Walsh, T.D. (2000). Seminars in Oncology, 27, 45-63.
(2) Walsh, T.D. (1990). J. Pain Symptom Manage., 5, 362-367.
(3) Holzer, P. (2012). Current Pharmaceutical Design, 18, 6010-6020.
(4) Vickery, R., et al. PainWeek 2012, Las Vegas, NV, September 5-8. Poster #121.

Exhibit 99.3

Poster 421
APS2013, New Orleans, LA
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No Evidence of Analgesic Interference or CNS Opioid Withdrawal for TD-1211 in a Phase 2b Study in Opioid-Induced Constipation

Ross Vickery(1), Lynn Webster(2), Yu-Ping Li(1), Ullrich Schwertschlag(1), Neil Singla(3), and Daniel Canafax(1)

(1) Theravance, Inc., South San Francisco, CA; (2) Lifetree Clinical Research, Inc., Salt Lake City, UT; (3) Lotus Clinical Research, Inc., Pasadena, CA

Introduction

- Opioid analgesics such as morphine continue to play a critical role in chronic cancer and non-cancer pain control.(1) Despite their effectiveness, opioids have significant drawbacks, notably the development of analgesic tolerance and physical dependence, sedation, respiratory depression and bowel dysfunction.(2)
- Opioid-induced constipation (OIC) is common, affecting up to 80% of patients receiving opioids for chronic non-cancer pain.(3)
- TD-1211 is an investigational, peripherally selective, mu-opioid receptor antagonist designed to alleviate gastrointestinal side effects of opioid therapy without affecting analgesia.
- Safety and efficacy results, including the primary and key secondary endpoints, from a 5-week, Phase 2b study in chronic non-cancer pain OIC patients have been previously reported.(4)
- Additional assessments on daily pain score, opioid dose, and central opioid withdrawal are reported here to demonstrate that TD-1211 is peripherally selective and does not impact centrally-mediated analgesia.

Methods

- A 5-week, double-blind, randomized, multi-center, placebo-controlled, parallel-group study was conducted in chronic non-cancer pain patients with OIC, defined as ≤5 spontaneous bowel movements (SBMs) over a 2-week baseline period and at least one additional symptom of constipation in at least 25% of the bowel movements.
- For the first 4 days of dosing, patients randomized to TD-1211 received 5mg daily and on Day 5, remained at 5mg or were dose-escalated to 10mg or 15mg daily for the remainder of the treatment period. Patients randomized to placebo received placebo for all 5 weeks.
- For at least 14 days prior to Day 1, patients were on a stable chronic opioid regimen, with a total daily dose of ≥30mg morphine equivalent units (MEU).
- Patients were required to stop laxatives and bowel regimens, except protocol-permitted rescue bisacodyl use, throughout the study.
- Electronic diaries collected frequency, timing, and symptoms of bowel movements; use of laxatives and opioids; daily pain scores; and satisfaction / quality of life metrics.
- The Clinician Opiate Withdrawal Scale (COWS) was used to assess symptoms of opioid withdraw at baseline and on Day 1 and Day 35.
- The primary efficacy endpoint was the change from baseline in weekly average complete spontaneous bowel movements (CSBMs) over weeks 2-5 of treatment.
- Week 1 was excluded from the primary analysis in order to confirm durability of response and predictability of longer term efficacy studies.

Results

Patient baseline characteristics

- 217 patients were randomized.

Opioid Use

- Majority of patients were on opioids for >3 years.
- Mean and median baseline daily oral opioid dose were 145 and 89 MEU, respectively, with a range of 30-1740 MEU.
- Subjects were on a representative spectrum of opioids.
- Back pain was the most commonly reported reason for chronic opioid use.

OIC

- Mean duration of OIC was 6 years.
- Mean baseline SBMs/week was 1.1-1.2.
- Mean satisfaction with ability to manage OIC was 3.0 (on 1-6 scale); 45% of patients were notably dissatisfied (score ≤2).
- 20% of patients reported sometimes taking less pain medication (typically a few days each month) because of OIC.

Primary efficacy endpoint

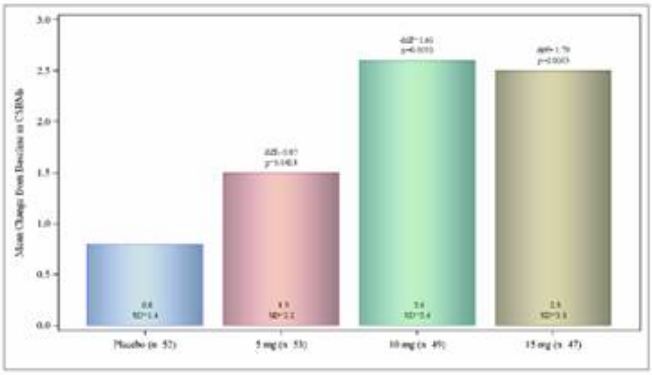
- All doses of TD-1211 achieved statistical significance for the change from baseline in weekly average CSBMs over weeks 2-5 of treatment. (**Figure 1**).

Measures demonstrating no evidence of analgesic interference

- The mean average daily pain score (0 - 10 VAS with 10 as worst imaginable pain) was 5.9 - 6.1 across treatment groups at baseline, and the change from baseline at Week 5 ranged from -0.7 to 0.1 across the 4 treatment groups (**Figure 2**).
- The mean change from baseline in daily opioid dose at Week 5 was -6, -8.9, and -4.3 MEU for the 5, 10, and 15mg TD-1211 treatment groups, respectively, compared with +4.8 MEU for placebo (**Figure 3**).

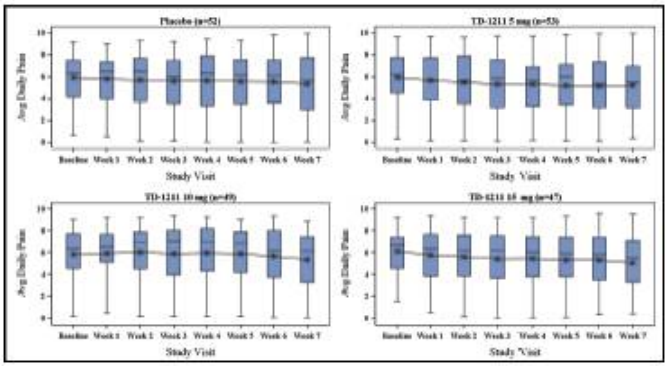
· On the COWS, with a maximum possible score of 48, the maximum post-treatment score reported was 6 for patients receiving TD-1211 (2 patients) and placebo (3 patients), indicating no evidence of CNS withdrawal. (One patient in the 15mg TD-1211 group had a score of 7 at baseline.) (**Figure 4**)

Figure 1: Primary Efficacy Endpoint: Change from Baseline in Weekly Average CSBMs over Weeks 2-5



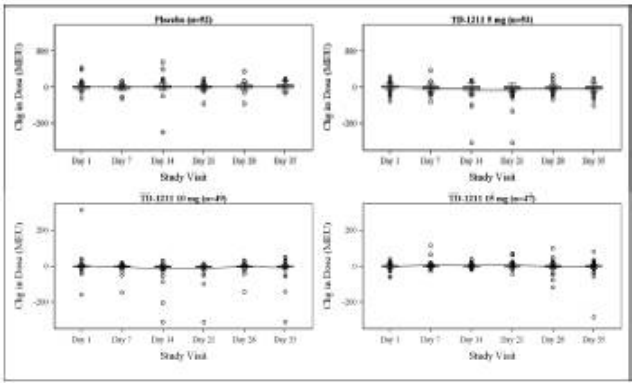
Efficacy Analysis (EA) Population, diff = Least Squares (LS) Mean Differences from placebo

Figure 2: Average Daily Pain Scores Per Week



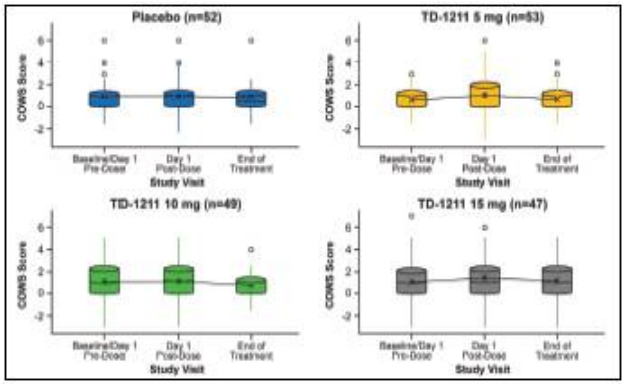
Efficacy Analysis (EA) Population. Weeks 6+7 = follow-up period. Asterisk =mean. Black line = median. Blue box = upper and lower quartiles. Whiskers = minimum and maximum score range.

Figure 3: Mean Change from Baseline in Daily Opioid Use on Study Visit Days



Efficacy Analysis (EA) Population. x = mean. Black line = median. Box = upper and lower quartiles. Whiskers = Q1 - 1.5*IQR, Q3 + 1.5*IQR, where IQR = Q3-Q1. Circles = outliers beyond the whisker range.

Figure 4: Clinician Opiate Withdrawal Scale



Efficacy Analysis (EA) Population. x = mean. Black line = median. Cylinder = upper and lower quartiles. Whiskers = Q1 - 1.5*IQR, Q3 + 1.5*IQR, where IQR = Q3-Q1. Circles = outliers beyond the whisker range.

Table 1: GI-Related Adverse Events Occurring in at Least 2 Patients in Any Group

		TD-1211			
Safety Population	**Placebo (N=54)**	**5 mg (N=56)**	**10 mg (N=53)**	**15 mg (N=52)**	**All TD-1211 (N=161)**
No. of Patients and Percentage with GI AEs	11 (20.4%)	13 (23.2%)	15 (28.3%)	14 (26.9%)	42 (26.1%)
Abdominal Pain	6 (11.1%)	7 (12.5%)	6 (11.3%)	8 (15.4%)	21 (13.0%)
Abdominal Pain Upper	1 (1.9%)	2 (3.6%)	3 (5.7%)	2 (3.8%)	7 (4.3%)
Diarrhea	0	4 (7.1%)	6 (11.3%)	4 (7.7%)	14 (8.7%)
Flatulence	3 (5.6%)	1 (1.8%)	2 (3.8%)	1 (1.9%)	4 (2.5%)
Nausea	2 (3.7%)	4 (7.1%)	8 (15.1%)	3 (5.8%)	15 (9.3%)
Vomiting	1 (1.9%)	4 (7.1%)	1 (1.9%)	0	5 (3.1%)

Tolerability and Safety

- TD-1211 was generally well tolerated, with overall treatment emergent adverse events (TEAEs) similar between TD-1211 and placebo and gastrointestinal (GI) TEAEs predominant. **(Table 1)**.
- The majority of treatment-related GI AEs were associated with initiation of treatment, resolved within a few days, and were mild or moderate.
- No treatment-related serious adverse events (SAEs) were reported.
- No clinically significant laboratory, ECG, or vital sign abnormalities were observed.

TD-1211 Conclusions

- 10mg and 15mg demonstrated sustained, clinically meaningful response over the 5-week treatment period.
- Met primary endpoint of change from baseline in CSBMs / week in moderate to severely constipated OIC population.
- No evidence of interference with analgesia, as noted by stable average daily pain scores and daily opioid doses over the treatment period.
- No evidence of centrally-mediated opioid withdrawal.
- Generally well-tolerated with no treatment-related SAEs.

References

(1) Walsh, T.D. (2000). Seminars in Oncology, 27, 45-63.
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(4) Vickery, R., et al. PainWeek 2012, Las Vegas, NV, September 5-8. Poster #121.