Trevena, Inc. (TRVN)

Initiating Coverage at Market Outperform; Platform-EnABLEd Drug Developer Focused on Unmet Medical Needs

MARKET DATA

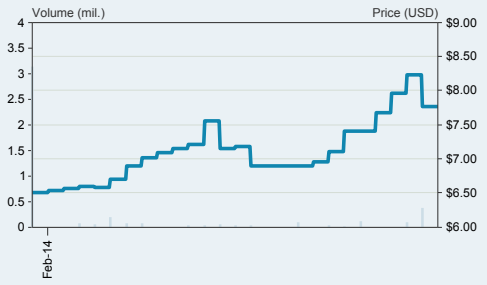
Price	$7.77
52-Week Range:	$6.35 - $8.98
Shares Out. (M):	25.7
Market Cap ($M):	$199.7
Average Daily Vol. (000):	372.0
Cash (M):	$107
Cash/Share:	$4.15
Enterprise Value (M):	$93

Source: Thomson Reuters and JMP Securities LLC

FY DEC		2013E	2014E	2015E
Revenue ($M)	1Q	--	$0.0	--
	2Q	--	$0.0	--
	3Q	--	$0.0	--
	4Q	--	$0.0	--
	FY	**$0.2**	**$0.0**	**$0.0**
EPS	1Q	--	($0.33)	--
	2Q	--	($0.50)	--
	3Q	--	($0.66)	--
	4Q	--	($0.65)	--
	FY	**($28.96)**	**($2.14)**	**($2.17)**
	P/E	NM	NM	NM

Source: Company reports and JMP Securities LLC

STOCK PRICE PERFORMANCE



MARKET OUTPERFORM | Price: $7.77 | Target Price: $18.00

INVESTMENT HIGHLIGHTS

We are initiating coverage on Trevena, Inc. with a Market Outperform rating and $18 price target. Trevena is a platform-enabled drug development company focused on the development of novel drugs with validated therapeutic targets where current treatment options are limited by safety or efficacy constraints. The company's lead development candidates, TRV130 and TRV027, are in Phase 2 development for the treatment of pain in the hospital setting and heart failure, respectively, and both have already demonstrated clinical proof-of-concept, in our view. Trevena completed its IPO on January 31, 2014 and we anticipate multiple clinical catalysts over the next 12-18 months that could drive continued value appreciation for shareholders. Our $18 price target is derived through a sum-of-the parts analysis for TRV130 and TRV027.

Drug discovery platform driven by Nobel Prize-winning science. Trevena is developing novel drugs discovered through its "biased ligand" platform. These drugs target G-protein coupled receptors (GPCRs), a class of cell surface receptors that are the target of more than 30% of current therapeutics. The signaling pathways regulated through GPCRs are responsible for a drug's efficacy and safety profiles. Trevena, expanding upon the Nobel Prize-winning science of Dr. Robert Lefkowitz at the Duke University Medical Center, has identified that GPCRs regulate multiple signaling pathways, of which some pathways may contribute more toward a beneficial therapeutic effect and others have a greater impact on adverse safety or tolerability effects. Furthermore, though its ABLE platform, the company has demonstrated the ability to identify drug candidates that are "biased" regulators of these different pathways and, therefore, have the potential to improve efficacy, or to limit adverse effects through an already-validated GPCR therapeutic target.

Lead development candidates address large commercial opportunities with potential to differentiate vs. current therapies. Trevena is focused on developing drug candidates for GPCRs that have already been validated as therapeutic targets. TRV130 is a biased ligand for the μ-opioid receptor, a well-validated target for the treatment of pain. We believe this drug candidate has the potential to achieve equivalent or better pain relief than current opioid drugs, while avoiding or minimizing key safety and tolerability limitations, namely respiratory depression and nausea/constipation. TRV027 is a biased ligand for AT1R, a known mediator of the renin angiotensin system (RAS). RAS has been viewed as an attractive therapeutic target for the treatment of acute heart failure but has previously been limited for drug development due to hypertensive adverse effects. We believe TRV027 has the potential to preserve cardiac performance while avoiding concerns of increased blood pressure.

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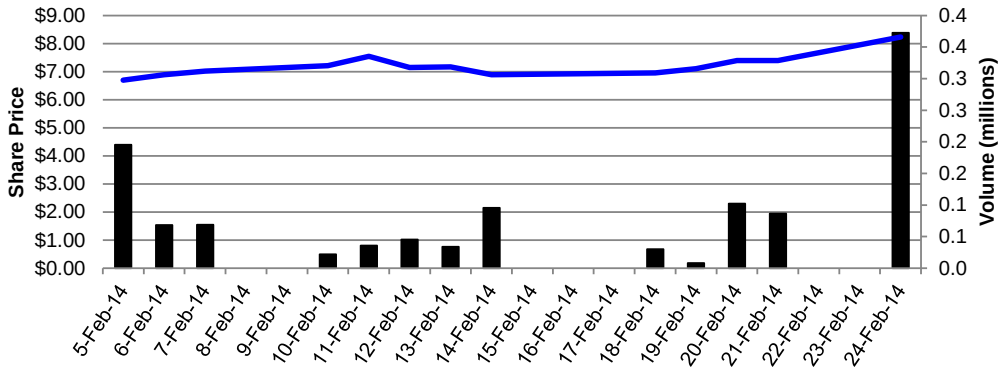
COMPANY DESCRIPTION

Trevena is a clinical-stage biopharmaceutical company based in King of Prussia, PA, focused on the discovery and development of small molecule and peptide G-protein coupled receptor (GPCR) biased ligands. The company was established in 2007 with the aim of translating groundbreaking academic research on GPCR signaling into a new generation of medicines. The company has two programs in clinical development: TRV027, currently in Phase 2 clinical testing for the treatment of acute heart failure, and TRV130, currently completing Phase 2 testing for the treatment of postoperative pain. In addition, Trevena has built an early-stage portfolio of drug discovery programs currently in lead optimization, including TRV734, currently in pre-clinical testing for oral treatment of acute and chronic pain.

In January 2014, Trevena completed its initial public offering, raising net proceeds of approximately $60MM through the sale of 9.25 million shares of common stock at a price of $7 per share. Following the completion of this offering, Trevena had approximately 25.7 million common shares outstanding with pro forma (9/30/2013) cash of $106MM and no debt. The proceeds from the IPO are intended to fund the development of TRV027, TRV130, and TRV734, as well as additional pre-clinical programs and for general working capital and corporate purposes.

FIGURE 1. TRVN Historical Stock Chart



Source: Thomson Reuters

KEY UPCOMING MILESTONES

2Q14	TRV130	Initiation of Phase 2 trial in postoperative subjects (bunionectomy)
3Q14	TRV734	Top-line results from Phase 1 trial
2H14	TRV130	Initiation of two Phase 2 safety and tolerability trials vs. μ-opioid agonists
1Q15	TRV130	Top-line results from Phase 2 trial in postoperative subjects
2H15	TRV130	Top-line results from Phase 2 safety and tolerability trials
2H15	TRV027	Top-line results from Phase 2b BLAST-AHF trial

INVESTMENT THESIS

Platform-enabled drug developer focused on novel and differentiated therapies for unmet medical needs. Trevena is a biopharmaceutical company that is developing new drugs based on its proprietary platform to enable better/safer clinical profiles for validated therapeutic targets. The platform is focused on G-protein coupled receptors (GPCRs), a large family of cell surface receptors that trigger molecular signaling pathways. Building on the Nobel Prize-winning research of Dr. Robert Lefkowitz at the Duke University Medical Center, Trevena is developing "biased ligands". These biased ligands are able to differentially activate or inhibit the separate signaling pathways of GPCRs and, in doing so, can separately impact safety and efficacy.

Lead candidates address blockbuster market opportunities. Trevena has two clinical-stage development candidates that target large and attractive commercial opportunities where unmet medical needs remain, heart failure and pain. Both of these candidates have demonstrated positive clinical proof-of-concept and are progressing into later-stage trials. The company's platform technology is continuing to produce drug candidates and we expect additional programs to enter clinical development in 2014 and 2015.

TRV130 could be transformative in the hospital pain setting. TRV130 is being developed as a first-line intravenous treatment for pain in the hospital and outpatient settings. The product candidate is a small molecule μ-opioid agonist, biased for the G protein pathway. The μ-opioid receptor is a well-established target for pain medications in the opiate class including morphine and fentanyl. The primary advantage of TRV130 is that it has the potential for potent pain relief, equivalent or greater than current opioid drugs, without the safety risk of respiratory depression and the tolerability constraint of constipation. Recent results from a Phase 1b trial demonstrated superior analgesia to a high dose of morphine, while causing less respiratory depression, nausea, and vomiting. A Phase 2 trial for TRV130 in the post-operative pain setting is expected to begin in 2Q14, with results expected in 1Q15. We conservatively estimate that the U.S. net sales potential for TRV130 in the hospital and outpatient settings is $600-$800MM by 2024 (sixth full year post-launch), with a similar amount ex-U.S.

TRV027 in Phase 2 trials for heart failure; Forest has already bought an option to partner the asset. TRV027 is being developed as a first-line treatment for acute heart failure (AHF) patients, in combination with standard diuretic therapy. There are over 20 million people living with heart failure in the U.S. and Europe and current therapies are limited by unfavorable safety and tolerability profiles. TRV027 is an intravenously injected peptide that targets the angiotensin II type 1 receptor (AT1R). AT1R is a validated target in heart failure and stimulating this receptor is known to enhance cardiac function; however, it also increases blood pressure and causes fluid retention which strains the heart and damages the kidneys, resulting in multi-organ damage. In a 33-patient Phase 2a trial, TRV027 rapidly reduced blood pressure and preserved renal, or kidney, function, while preserving cardiac performance. The company initiated a Phase 2b trial earlier in January 2014 and results are anticipated in 2H15. We believe the commercial opportunity for TRV027 could approach $1bil in the U.S. by 2024 (sixth full year post-launch), with a similar amount ex-U.S.

VALUATION

We value Trevena through a sum-of-the-parts NPV analysis of TRV130 in the hospital pain setting and TRV027 in heart failure. Our full revenue models and accompanying descriptions can be found on pages 13-16 for TRV130 and pages 23-25 for TRV027. Note that our valuation assumes the company commercializes TRV130 itself and that the option agreement with Forest is exercised for TRV027, with Trevena receiving royalties on global net sales.

We probability adjust our revenue projections to reflect clinical, regulatory, and commercial risks and apply a 15% discount rate to our NPV calculations to reflect the company's cost of capital. As summarized below, our price target reflects the ~25.7 million shares currently outstanding.

With a current market cap of ~$200MM and enterprise value of just under $100MM, we view TRVN as an attractive investment opportunity with multiple clinical catalysts over the coming 12-18 months that could drive substantial value accretion.

FIGURE 2. Trevena Sum-of-the-Parts NPV Valuation

	Peak revenue	Peak revenue year	Economics	Probability of success	Discount rate	NPV	NPV per share	Contribution
TRV130 sales	**1056.4**	**2026**	**100%**	**50%**	**15%**	**379.1**	**$14.73**	**80%**
U.S.	746.1	2026	100%	50%	15%	282.8	$10.99	60%
Europe	310.3	2026	100%	50%	15%	96.3	$3.74	20%
TRV027 royalties	**868.5**	**2026**	**17%**	**35%**	**15%**	**96.0**	**$3.73**	**20%**
U.S.	435.0	2026	18%	35%	15%	57.7	$2.24	12%
Europe	433.5	2026	16%	35%	15%	38.3	$1.49	8%
Price target							**$18.46**	**100%**

Source: JMP Securities LLC

Capital Structure

Following the completion of the January 2014 IPO, Trevena has approximately 25.7 million shares outstanding. An additional 1.4 million shares may be issued through the underwriters green shoe option. A further ~4 million shares are excluded from this total and may be issued primarily relating to stock options and equity incentive plans.

Balance Sheet

Following the completion of its IPO, Trevena had a pro forma cash position of $106MM. We view this as sufficient to fund operations through key valuation-inflecting catalysts for the TRV130 and TRV027 development programs. Specifically, we believe current cash will fund Phase 2 development of TRV130 and TRV027, as well as the advancement of additional platform-driven development candidates, including TRV734, into the clinic in 2014 and 2015.

INVESTMENT RISKS

Clinical risk. Trevena may not be successful in the full development and launch of its product candidates. There may be efficacy or safety issues related to product candidates undergoing clinical trials that would preclude continued development.

Regulatory risk. The FDA and/or other ex-U.S. regulatory agencies could reject any of the company's, or its partners', future regulatory filings or require additional studies prior to granting approval.

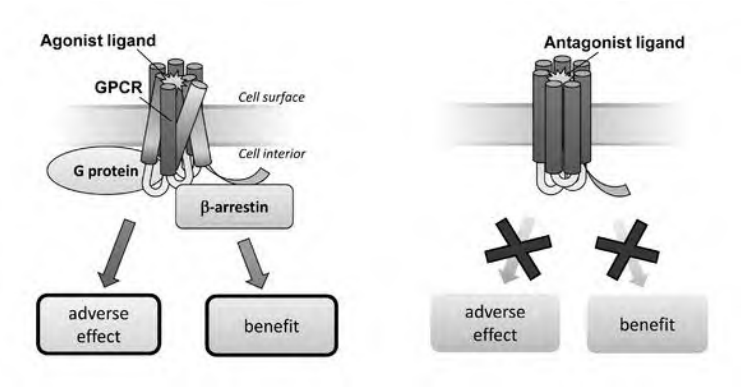
Industry risk. Given the competitive landscape in the biotechnology space, another company may come out with a more efficacious, less expensive product that could take significant market share away from Trevena's products, challenging the company's chances for success.

Balance sheet risk. The company has a history of losses and has not yet established a track record of consistent profitability. While we project that the company will not need to raise additional capital to maintain profitability, it may be necessary to do so to fund the business model. Trevena had a pro forma cash position as of September 30, 2013 of approximately $106MM and we project that the company will end 2014 with cash of $60.8MM.

ABLE PLATFORM – BIASED LIGANDS

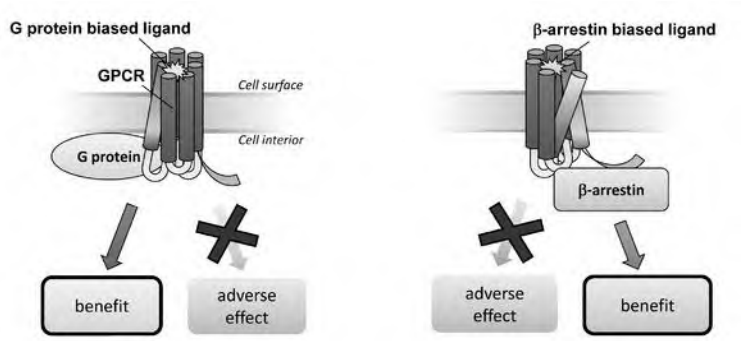
Trevena's development programs are based upon its proprietary Advanced Biased Ligand Explorer (ABLE) platform. This platform enables the identification of novel GPCR-targeted "biased ligands" with attractive pharmaceutical properties. G protein coupled receptors (GPCRs) make up the largest family of cell surface receptors and regulated cellular signaling pathways. GPCRs primarily trigger two signaling pathways, G protein and β-arrestin, which are involved in a wide variety of cellular function and disease cascade processes. More than 30% of currently marketed therapeutics target GPCRs either by activating or inhibiting both the G protein and β-arrestin pathways (Figure 2). These pathways are responsible for both desirable therapeutic effects and undesirable safety or tolerability side effects. In contrast, biased ligands selectively and separately modulate these two GPCR signaling pathways (Figure 3). Therefore, biased ligands may have the potential to provide differentiated and superior therapeutic profiles compared to currently available GPCR-targeted drugs.

FIGURE 3. Current Target-Specificity Approach



Source: Company reports

FIGURE 4. Biased Ligand Signal Specificity Approach



Source: Company reports

The biased ligand concept was developed by the company's scientific founder, Dr. Robert Lefkowitz, recipient of the 2012 Nobel Prize in Chemistry for his work in understanding the G protein coupled receptor system and its application in medical science, including elucidation of the multiple pathways that a GPCR engages. Dr. Lefkowitz is currently a James B. Duke Professor of Medicine and Biochemistry at Duke University Medical Center and an Investigator for the Howard Hughes Medical Institute. He leads Trevena's Scientific Advisory Board.

Based on Dr. Lefkowitz's work, Trevena has developed in vitro assays that can measure G protein and β-arrestin signaling from a receptor of interest and determine if a particular ligand is biased, and if so whether it is a G protein or β-arrestin biased ligand, and to what extent. These assays can also measure cellular responses resulting from signaling pathways and enable associations to be made between molecular signaling and pharmacological responses (i.e., provide information regarding the therapeutic benefits and adverse effects driven by one or both of the G protein or β-arrestin pathways).

Through the ABLE platform, Trevena has advanced multiple biased ligand candidates into pre-clinical and clinical development. The company's lead development program is TRV130, an intravenously administered μ-opioid receptor agonist in Phase 2 development for post-operative pain. The company's second clinical candidate is TRV027, in Phase 2 development as a treatment for heart failure. TRV027 is a peptide β-arrestin biased ligand that targets the angiotensin II type 1 receptor (AT1R), a GPCR expressed on cells within the cardiovascular system. A third candidate, TRV734, also a μ-opioid receptor agonist but available for oral administration, began Phase 1 development in 1Q14. The company is also in pre-clinical development stages for δ-opioid receptor and K-opioid receptor agonists. The company's pipeline is summarized in Figure 5.

FIGURE 5. Trevena Pipeline

Asset	Target	Route of Administration	Indication	Development stage	Ownership
Cardiovascular					
TRV027	angiotensin II type 1 receptor (AT1R)	IV	Acute heart failure (AHF)	Phase 2	Forest Laboratories (Collaboration)
CNS					
TRV130	μ-opioid receptor (MOR)	IV	Post-operative pain	Phase 1	Wholly owned
TRV734	μ-opioid receptor (MOR)	Oral	Acute/chronic pain	Phase 1	Wholly owned
n/a	δ-opioid receptor	Oral	Parkinson's disease, depression, pain	Lead optimization	Wholly owned
n/a	κ-opioid receptor	Oral	Neuropathic pain	Lead optimization	Wholly owned

Source: Company data

TRV130 FOR ACUTE PAIN

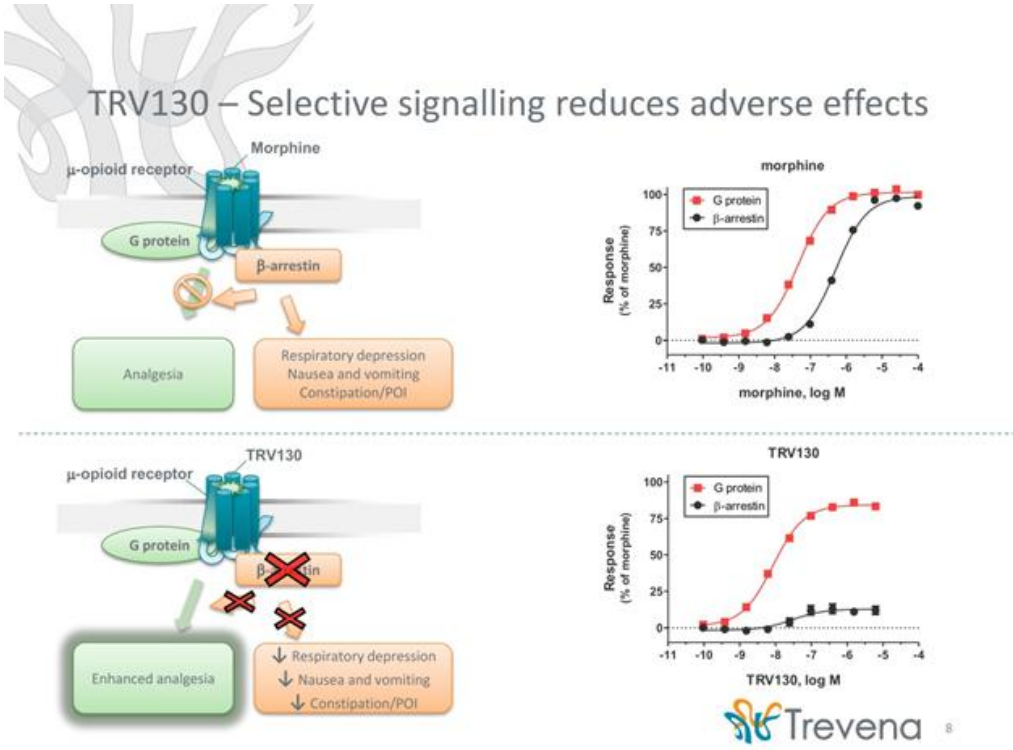
TRV130 is an intravenously administered small molecule G protein biased ligand that targets the μ-opioid receptor. The drug candidate is being developed as a first-line treatment for moderate to severe acute pain in the hospital setting. We believe that TRV130 has the potential to provide potent pain relief, at least equivalent to standard of care IV opioids, with less respiratory depression and gastrointestinal side effects.

Trevena has completed four Phase 1 trials, including a placebo-controlled Phase 1b trial using a validated cold pain test design that demonstrated superior analgesia to morphine at higher doses and a more favorable safety/tolerability profile. The company plans to initiate two Phase 2 trials in 2014 (bunionectomy/soft tissue surgery) that could inform advancement to Phase 3 development in 2015.

Mechanism of action and commercial opportunity

The μ-opioid receptor is a well-validated target for pain therapy; however, key to developing a new product is the potential to differentiate from current opioid drugs that provide potent pain relief. The primary limitation of opioids, and therefore the potential to differentiate, is safety/tolerability. The key safety concern is respiratory depression and more prominent tolerability concerns are nausea/vomiting and constipation.

FIGURE 6. Selective GPCR Signaling with TRV130



Source: Company reports

Through in vitro studies, Trevena has generated evidence supporting that analgesia is primarily driven through activation of the G-protein pathway of the μ-opioid GPCR. Furthermore, the key limiting adverse events summarized above are driven through the activation of the β-arrestin pathway. Using its ABLE platform, Trevena designed TRV130 as a G-protein biased ligand, with the potential to selectively provide potent pain relief while reducing side effects. As shown in Figure 6, morphine activates both the G-protein and β-arrestin pathways at therapeutic doses, whereas TRV130 activates only the G-protein pathway.

Clinical development program

Trevena has completed four Phase 1 trials evaluating TRV130 in healthy subjects and intends to initiate two Phase 2 trials in 2014. The completed trials include:

- A Phase 1b proof-of-concept exploratory trial in healthy subjects using an evoked-pain model to evaluate analgesic efficacy of TRV130 compared to a high dose of morphine, as well as evaluated nausea, vomiting, and respiratory depression.
- A three-part, Phase 1 trial in healthy subjects to evaluate the pharmacokinetics and tolerability of TRV130.
- A Phase 1 IV bolus trial in healthy subjects to expand the dataset generated in Part C of the three-part trial with respect to TRV130's pharmacokinetics and tolerability administered as an IV bolus, as well as pupil constriction.
- A Phase 1 drug-drug interaction study to evaluate the safety and tolerability of TRV130 when administered with an inhibitor of one of the primary pathways of TRV130 metabolism.

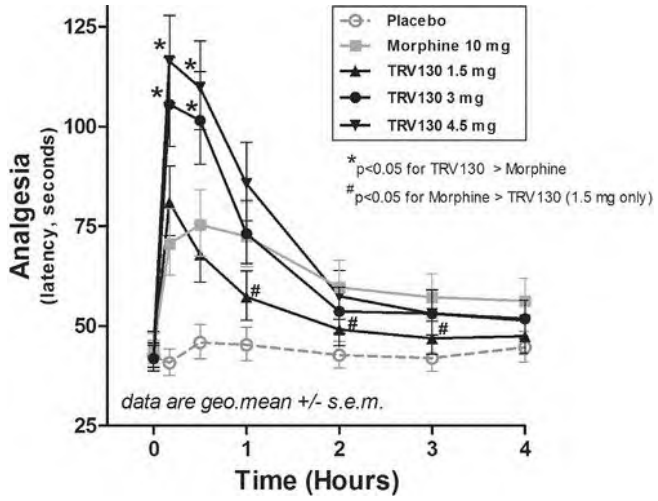
Phase 1b proof-of-concept trial

The most important data generated to date for TRV130, in our view, are from the Phase 1b proof-of-concept trial that evaluated the drug's safety and efficacy using an evoked-pain model.

The trial compared the efficacy, safety, and tolerability of TRV130 versus a high dose of morphine (10 mg) in a double-blind, five-period, crossover study. This trial enrolled 30 healthy male subjects randomized to receive a two-minute infusion of three dose levels of TRV130 (1.5 mg, 3.0 mg, and 4.5 mg), 10 mg morphine, and placebo. Analgesic effects were evaluated using an evoked-pain model (i.e., the cold pain test), which is a validated model to evaluate opioid effectiveness. The test measures the time that a subject can maintain their hand in a temperature-controlled cold water bath. Visual analog scale measurements of nausea were also employed and respiratory depression was measured through ventilatory response to hypercapnia, another well-known experimental model.

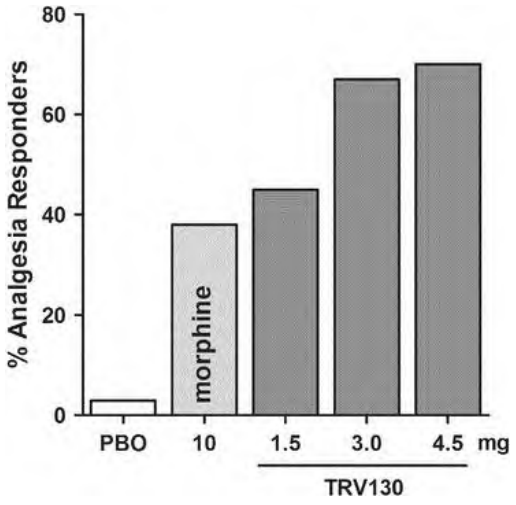
The results demonstrated that at both the 3.0 mg and 4.5 mg doses, TRV130 showed statistically significant superior efficacy versus a 10 mg morphine dose at the 10 and 30 minute time points after dosing ($p < 0.05$). The durability of the analgesic effect was similar to morphine (Figure 7). In addition, the time to peak effect was more rapid than morphine. Moreover, there were a higher number of responders at the 3.0 mg and 4.5 mg dose levels compared to morphine (Figure 8). A responder was defined as a subject who experienced a doubling of latency as compared to pre-dose baseline.

FIGURE 7. Analgesic Effect of TRV130 as Compared to Morphine in an Evoked-Pain Model



Source: Company reports

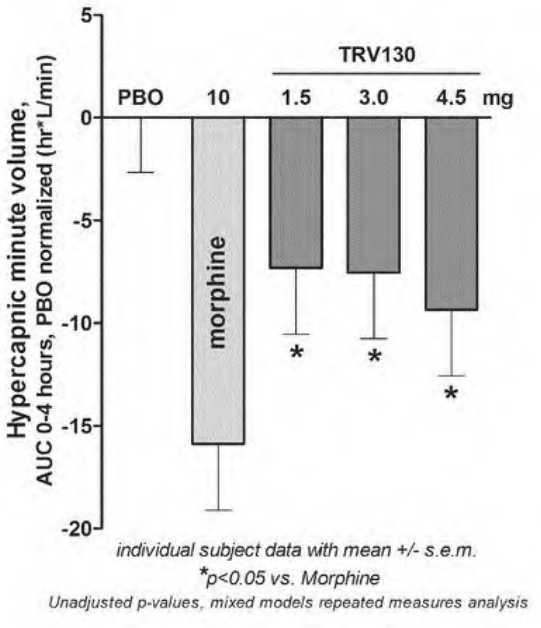
FIGURE 8. Higher Proportion of Responders to TRV130 as Compared to Morphine in an Evoked-Pain Model



Source: Company reports

TRV130 was generally well tolerated. Subjects receiving TRV130 had less nausea and less vomiting at the 1.5 mg and 3.0 mg doses as compared to a 10 mg dose of morphine. All doses of TRV130 showed less respiratory depression compared to morphine ($p<0.05$), measured as minute volume (MV), (i.e., area under the curve over four hours) (Figure 9). MV is a product of respiratory rate and tidal volume, or the amount of air exhaled in a single breath, and thereby captures the body's ability to expel carbon dioxide. The 3.0 mg TRV130 dose demonstrated superior efficacy, less nausea, less vomiting, and less respiratory depression in this trial as compared to 10 mg morphine.

FIGURE 9. Less Respiratory Depression with TRV130 as Compared to Morphine



Source: Company reports

Planned Phase 2 trials

The regulatory path for novel pain therapeutics in the hospital setting is well defined. Trevena is planning to initiate a Phase 2 program for TRV130 in 1H14 investigating the analgesic efficacy, safety, and tolerability profile compared to existing opioid pain medications. The first trial will be a study in bunionectomy patients. The trial is expected to begin in 2Q14 and will enroll approximately 400 patients. The trial is designed to allow for an adaptive dose selection to identify the optimal dose of TRV130 compared to morphine and will be powered to demonstrate superior pain relief vs. morphine. Results are expected in 1Q15 and may inform the progression of this development program into Phase 3 trials.

A second Phase 2 trial in patients following soft tissue surgery is expected to be initiated in 4Q14. The trial will be designed to support a potentially differentiated tolerability profile and further inform Phase 3 design. Results from this trial are expected in 4Q15, however, are not critical to the initiation of a Phase 3 program.

Commercial opportunity in the IV pain market

According to IMS Health, in 2010 in the U.S., there were approximately 30 million reimbursement claims made for IV opioids by hospitals. Of these, 14 million were inpatient claims and 16 million were outpatient claims. The IMS Health reimbursement data show that 75% of inpatient and 50% of outpatient claims for IV opioids were surgery-related in 2010. Trevena anticipates that the initial market opportunity for TRV130 would be the acute care, hospital setting, with a focus on postoperative pain.

The World Health Organization (WHO) estimates that more than 230 million major surgical procedures are performed worldwide annually. In 2010 in the U.S., over 30 million hospital inpatient surgical procedures were recorded by NHDS, with a similar number performed collectively in France, Germany, the U.K., Italy, and Spain. According to the U.S. Centers for Disease Control and Prevention (CDC), in 2006 in the U.S. there were an additional 20 million outpatient surgical procedures in U.S. hospitals and an additional 14 million procedures in ambulatory surgical centers.

Current treatment options

Opioids remain the mainstay treatment of moderate to severe, acute postoperative pain, these include morphine, fentanyl, and hydromorphone. As noted above, these drugs are associated with respiratory depression with reduced respiratory rate and reduced tidal volume, (i.e., the amount of air inhaled or exhaled in one breath). The risk of respiratory depression is the primary concern of physicians when prescribing an opioid analgesic and drives reluctance to increase the opioid dose. Trevena estimates that in the U.S. approximately 80,000 cases of opioid-induced respiratory depression occur each year in hospitalized patients, with an increased risk in patients who are obese or who have chronic obstructive pulmonary disease (COPD) and sleep apnea.

Additional side effects include nausea, vomiting, and constipation. Constipation represents a burden to both the patient and hospital as surgical patients typically are not discharged until they have had a meal or a bowel movement. Furthermore, surgery involving interruption of movement of the intestines can lead to postoperative ileus (POI), where the bowel enters spasm and stops passing food and waste. POI is exacerbated by anesthetics and opioid analgesics and occurs in at least 10% of patients following invasive abdominal procedures.

Potential for TRV130 to provide a differentiated treatment option

While opioids are the most effective class of analgesics currently available, they are limited by unfavorable safety and tolerability effects. We believe TRV130 may have differentiating attributes in terms of both efficacy and safety compared to existing opioid treatments for postoperative pain. As discussed above, the Phase 1b evoked-pain trial showed that TRV130 demonstrated superior analgesia compared to a high dose of morphine while causing less respiratory depression, and caused less nausea and less vomiting at a lower dose with comparable efficacy to morphine. Additionally pre-clinical studies have shown that TRV130 delivered maximal efficacy at 5 minutes after dosing versus ~30 minutes for morphine. This was supported by Phase 1 results showing analgesic effect at 10 minutes after dosing, the first practical data collection point.

TRV130 Revenue Model

We project revenues for TRV130 in both the U.S. (Figure 10) and Europe (Figure 11) in four settings, including surgical and non-surgical uses in both inpatient and outpatient settings. A description of our assumptions is detailed below.

U.S. Revenue Projections

U.S. Hospital Inpatient Surgical: According to third-party claims data, there were approximately 10.5 million claims for IV opioids in the U.S. hospital inpatient surgical setting in 2010, and we assume 2% growth per year. We project market penetration of 0.5% in 2018, ramping to 8% by 2023 and remaining flat thereafter. We estimate a cost per day of $75 beginning in 2018, increasing annually at a rate of 3%, and two days of dosing per patient. According to these assumptions, we project 2026 revenues of $219MM.

U.S. Hospital Inpatient Non-Surgical: There were approximately 3.5 million claims for IV opioids in this setting in 2010. We assume 3% growth per year thereafter. We project market penetration of 0.5% in 2018, ramping to 12% by 2024 and remaining flat thereafter. We estimate a cost per day of $75, increasing annually at a rate of 3%, and two days of dosing per patient. According to these assumptions, we project 2026 revenues of $128MM.

U.S. Hospital Outpatient Surgical: There were approximately 8.0 million claims for IV opioids in the U.S. hospital outpatient surgical setting in 2010, and we assume 3% growth per year. We project market penetration of 0.5% in 2018, ramping to 12% by 2024 and remaining flat in subsequent years. We estimate a cost per day of $75, increasing annually at a rate of 3%, and two days of dosing per patient. According to these assumptions, we project 2026 revenues of $293MM.

U.S. Hospital Outpatient Non-Surgical: There were approximately 8.0 million claims for IV opioids in the U.S. hospital outpatient non-surgical setting in 2010, and we assume 3% annual growth thereafter. We project market penetration of 0.5% in 2018, ramping to 12% by 2024 and remaining flat thereafter. We estimate a cost per day of $75, increasing annually at a rate of 3%, and two days of dosing per patient. According to these assumptions, we project 2026 revenues of $293MM.

We estimate total gross revenue in the U.S. in 2026 of $933MM. We assume a gross-to-net adjustment of 20% throughout our forecast period, resulting in total net revenues in the U.S. in 2026 of $746MM.

FIGURE 10. TRV130 U.S. Revenue Model

U.S. Hospital Inpatient Surgical	2010	2011	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026
Patient claims for IV opioids	10,500,000	10,710,000	12,061,200	12,302,424	12,548,472	12,799,441	13,055,430	13,316,539	13,582,870	13,854,527	14,131,618	14,414,250
% growth		2.0%	2.0%	2.0%	2.0%	2.0%	2.0%	2.0%	2.0%	2.0%	2.0%	2.0%
Number of patients treated with TRV130				61,512	125,485	383,983	783,326	932,158	1,086,630	1,108,362	1,130,529	1,153,140
% penetration				***0.5%***	***1.0%***	***3.0%***	***6.0%***	***7.0%***	***8.0%***	***8.0%***	***8.0%***	***8.0%***
Total cost per patient				$150	$155	$159	$164	$169	$174	$179	$184	$190
Cost per day	$0.00	$0.00	$0.00	$75.00	$77.25	$79.57	$81.95	$84.41	$86.95	$89.55	$92.24	$95.01
Annual price increase					3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%
Number of days of dosing				2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0
Total revenue ($MM)				**9.2**	**19.4**	**61.1**	**128.4**	**157.4**	**189.0**	**198.5**	**208.6**	**219.1**

U.S. Hospital Inpatient Non-surgical	2010	2011	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026
Patient claims for IV opioids	3,500,000	3,605,000	4,304,559	4,433,695	4,566,706	4,703,707	4,844,819	4,990,163	5,139,868	5,294,064	5,452,886	5,616,473
% growth		3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%
Number of patients treated with TRV130				22,168	91,334	188,148	387,585	499,016	565,385	635,288	654,346	673,977
% penetration				***0.5%***	***2.0%***	***4.0%***	***8.0%***	***10.0%***	***11.0%***	***12.0%***	***12.0%***	***12.0%***
Total cost per patient				$150	$155	$159	$164	$169	$174	$179	$184	$190
Cost per day				$75.00	$77.25	$79.57	$81.95	$84.41	$86.95	$89.55	$92.24	$95.01
Annual price increase					3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%
Number of days of dosing				2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0
Total revenue ($MM)				**3.3**	**14.1**	**29.9**	**63.5**	**84.2**	**98.3**	**113.8**	**120.7**	**128.1**

U.S. Hospital Outpatient Surgical	2010	2011	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026
Patient claims for IV opioids	8,000,000	8,240,000	9,838,991	10,134,161	10,438,185	10,751,331	11,073,871	11,406,087	11,748,270	12,100,718	12,463,739	12,837,652
% growth		3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%
Number of patients treated with TRV130				50,671	208,764	430,053	885,910	1,140,609	1,292,310	1,452,086	1,495,649	1,540,518
% penetration				***0.5%***	***2.0%***	***4.0%***	***8.0%***	***10.0%***	***11.0%***	***12.0%***	***12.0%***	***12.0%***
Total cost per patient				$150	$155	$159	$164	$169	$174	$179	$184	$190
Cost per day				$75.00	$77.25	$79.57	$81.95	$84.41	$86.95	$89.55	$92.24	$95.01
Annual price increase					3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%
Number of days of dosing				2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0
Total revenue ($MM)				**7.6**	**32.3**	**68.4**	**145.2**	**192.6**	**224.7**	**260.1**	**275.9**	**292.7**

U.S. Hospital Outpatient Non-surgical	2010	2011	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026
Patient claims for IV opioids	8,000,000	8,240,000	9,838,991	10,134,161	10,438,185	10,751,331	11,073,871	11,406,087	11,748,270	12,100,718	12,463,739	12,837,652
% growth		3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%
Number of patients treated with TRV130				50,671	208,764	430,053	885,910	1,140,609	1,292,310	1,452,086	1,495,649	1,540,518
% penetration				***0.5%***	***2.0%***	***4.0%***	***8.0%***	***10.0%***	***11.0%***	***12.0%***	***12.0%***	***12.0%***
Total cost per patient				$150	$155	$159	$164	$169	$174	$179	$184	$190
Cost per day				$75.00	$77.25	$79.57	$81.95	$84.41	$86.95	$89.55	$92.24	$95.01
Annual price increase					3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%
Number of days of dosing				2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0	2.0
Total revenue ($MM)				**7.6**	**32.3**	**68.4**	**145.2**	**192.6**	**224.7**	**260.1**	**275.9**	**292.7**

Total gross U.S. revenue ($MM)				**27.8**	**98.0**	**227.9**	**482.3**	**626.7**	**736.7**	**832.5**	**881.1**	**932.6**
Gross-to-net adjustment				*20.0%*	*20.0%*	*20.0%*	*20.0%*	*20.0%*	*20.0%*	*20.0%*	*20.0%*	*20.0%*
Total net U.S. revenue ($MM)				**22.2**	**78.4**	**182.3**	**385.9**	**501.4**	**589.4**	**666.0**	**704.9**	**746.1**

Source: JMP Securities LLC, Company reports

EU Revenue Projections

EU Hospital Inpatient Surgical: We assume a similar market size as in the U.S. for IV opioids in the EU hospital inpatient surgical setting in 2010, and we assume 3% annual growth. We project market penetration of 0.5% in 2019, ramping to 7% by 2024 and remaining flat thereafter. We estimate a cost per day of $59 beginning in 2019, increasing annually at a rate of 3%, and 2.2 days of dosing per patient. According to these assumptions, we project 2026 revenues of $187MM.

EU Hospital Inpatient Non-Surgical: There were approximately 3.5 million claims for IV opioids in this setting in 2010. We assume 3% growth per year thereafter. We project market penetration of 0.5% in 2019, ramping to 10% by 2024 and remaining flat thereafter. We estimate a cost per day of $59, increasing annually at a rate of 3%, and 2.2 days of dosing per patient. According to these assumptions, we project 2026 revenues of $89MM.

EU Hospital Outpatient Surgical: There were approximately 8.0 million claims for IV opioids in the EU hospital outpatient surgical setting in 2010, and we assume 3% growth per year. We project market penetration of 0.5% in 2019, ramping to 10% by 2024 and remaining flat in subsequent years. We estimate a cost per day of $57, increasing at an annual rate of 3%, and 0.6 days of dosing per patient. According to these assumptions, we project 2026 revenues of $56MM.

EU Hospital Outpatient Non-Surgical: There were approximately 8.0 million claims for IV opioids in the EU hospital outpatient non-surgical setting in 2010, and we assume 3% annual growth thereafter. We project market penetration of 0.5% in 2019, ramping to 10% by 2024 and remaining flat thereafter. We estimate a cost per day of $57, increasing annually at a rate of 3%, and 0.6 days of dosing per patient. According to these assumptions, we project 2026 revenues of $56MM.

We estimate total gross revenue in the EU in 2026 of $388MM. We assume a gross-to-net adjustment of 20% throughout our forecast period, resulting in total net revenues in the EU in 2026 of $310MM.

We forecast TRV130 worldwide gross revenue in 2026 of $1.32bn with net sales of $1.06bn.

FIGURE 11. TRV130 EU Revenue Model

EU Hospital Inpatient Surgical	2010	2011	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026
Patient claims for IV opioids	10,500,000	10,815,000	12,913,676	13,301,086	13,700,118	14,111,122	14,534,456	14,970,489	15,419,604	15,882,192	16,358,658	16,849,418
% growth		3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%
Number of patients treated with TRV130					68,501	141,111	436,034	748,524	925,176	1,111,753	1,145,106	1,179,459
% penetration				***0.0%***	***0.5%***	***1.0%***	***3.0%***	***5.0%***	***6.0%***	***7.0%***	***7.0%***	***7.0%***
Cost per day				$57.00	$58.71	$60.47	$62.29	$64.15	$66.08	$68.06	$70.10	$72.21
Annual price increase					3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%
Number of days of dosing				2.2	2.2	2.2	2.2	2.2	2.2	2.2	2.2	2.2
Total cost per patient				$125	$129	$133	$137	$141	$145	$150	$154	$159
Total revenue ($MM)				**0.0**	**8.8**	**18.8**	**59.7**	**105.6**	**134.5**	**166.5**	**176.6**	**187.4**

EU Hospital Inpatient Non-surgical	2010	2011	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026
Patient claims for IV opioids	3,500,000	3,605,000	4,304,559	4,433,695	4,566,706	4,703,707	4,844,819	4,990,163	5,139,868	5,294,064	5,452,886	5,616,473
% growth		3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%
Number of patients treated with TRV130					22,834	70,556	145,345	349,311	462,588	529,406	545,289	561,647
% penetration				***0.0%***	***0.5%***	***1.5%***	***3.0%***	***7.0%***	***9.0%***	***10.0%***	***10.0%***	***10.0%***
Cost per day				$57.00	$58.71	$60.47	$62.29	$64.15	$66.08	$68.06	$70.10	$72.21
Annual price increase					3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%
Number of days of dosing				2.2	2.2	2.2	2.2	2.2	2.2	2.2	2.2	2.2
Total cost per patient				$125	$129	$133	$137	$141	$145	$150	$154	$159
Total revenue ($MM)	**0.0**	**0.0**	**0.0**	**0.0**	**2.9**	**9.4**	**19.9**	**49.3**	**67.2**	**79.3**	**84.1**	**89.2**

EU Hospital Outpatient Surgical	2010	2011	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026
Patient claims for IV opioids	8,000,000	8,240,000	9,838,991	10,134,161	10,438,185	10,751,331	11,073,871	11,406,087	11,748,270	12,100,718	12,463,739	12,837,652
% growth		3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%
Number of patients treated with TRV130					52,191	161,270	332,216	798,426	1,057,344	1,210,072	1,246,374	1,283,765
% penetration				***0.0%***	***0.5%***	***1.5%***	***3.0%***	***7.0%***	***9.0%***	***10.0%***	***10.0%***	***10.0%***
Cost per day				$57.00	$58.71	$60.47	$62.29	$64.15	$66.08	$68.06	$70.10	$72.21
Annual price increase					3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%
Number of days of dosing				0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6
Total cost per patient				$34	$35	$36	$37	$38	$40	$41	$42	$43
Total revenue ($MM)				**0.0**	**1.8**	**5.9**	**12.4**	**30.7**	**41.9**	**49.4**	**52.4**	**55.6**

EU Hospital Outpatient Non-surgical	2010	2011	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026
Patient claims for IV opioids	8,000,000	8,240,000	9,838,991	10,134,161	10,438,185	10,751,331	11,073,871	11,406,087	11,748,270	12,100,718	12,463,739	12,837,652
% growth		3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%
Number of patients treated with TRV130					52,191	161,270	332,216	798,426	1,057,344	1,210,072	1,246,374	1,283,765
% penetration				***0.0%***	***0.5%***	***1.5%***	***3.0%***	***7.0%***	***9.0%***	***10.0%***	***10.0%***	***10.0%***
Cost per day				$57.00	$58.71	$60.47	$62.29	$64.15	$66.08	$68.06	$70.10	$72.21
Annual price increase					3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%
Number of days of dosing				0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6
Total cost per patient				$34	$35	$36	$37	$38	$40	$41	$42	$43
Total revenue ($MM)				**0.0**	**1.8**	**5.9**	**12.4**	**30.7**	**41.9**	**49.4**	**52.4**	**55.6**

Total gross EU revenue ($MM)				**0.0**	**15.5**	**39.9**	**104.5**	**216.4**	**285.6**	**344.6**	**365.6**	**387.8**
Gross-to-net adjustment				*20.0%*	*20.0%*	*20.0%*	*20.0%*	*20.0%*	*20.0%*	*20.0%*	*20.0%*	*20.0%*
Total net EU revenue ($MM)				**0.0**	**12.4**	**31.9**	**83.6**	**173.1**	**228.5**	**275.7**	**292.4**	**310.3**

Source: JMP Securities LLC, Company reports

TRV130 Intellectual property

Trevena's patent portfolio protecting TRV130 includes two pending U.S. patent applications claiming the compound, other compounds, and/or methods of making or using the same. If issued, the pending U.S. applications are estimated to expire no earlier than 2032, subject to extensions. A related PCT application was filed and national patent applications have been filed in a number of other countries. Any patents resulting from these national patent applications, if issued, are expected to expire no earlier than 2032, subject to any disclaimers or extensions.

TRV027 FOR HEART FAILURE

TRV027 is in Phase 2b development for acute heart failure (AHF). The drug candidate is a peptide β-arrestin biased ligand that targets the angiotensin II type 1 receptor (AT1R), a key mediator of the renin angiotensin system (RAS) and a validated therapeutic target for heart failure. The drug candidate is being developed as a first-line, intravenous treatment in combination with standard diuretic therapy for patients with AHF. Based on the drug's rational design and pre-clinical and clinical results seen to date, we believe TRV027 could improve AHF symptoms and shorten the length of hospital stay and potentially lower readmission rates and mortality rates after hospital discharge.

Trevena has completed three clinical trials of TRV027, including two Phase 1 trials and a Phase 2a study, as described below. These trials have demonstrated an encouraging clinical profile to date, rapidly reducing blood pressure and preserving renal function, while preserving cardiac performance. In January 2014, the company initiated a Phase 2b study and results are expected in 4Q15. In May 2013, Trevena and Forest Laboratories entered into an option and license agreement, granting Forest the option of licensing TRV027 following the completion of this Phase 2b trial. The terms of the deal are described below.

Mechanism of action and opportunity in heart failure

Heart failure is a chronic, progressive disease in which the heart is unable to pump sufficient blood around the body to meet its needs for oxygen. The heart compensates for this insufficiency by enlarging and developing more muscle mass, and the body further compensates to increase or maintain blood pressure. Activation of the renin angiotensin system (RAS) via angiotensin II is a well-validated compensatory mechanism in heart failure, in order to maintain blood pressure and flow. It is a reaction to the heart's inability to generate sufficient blood flow, and therefore oxygen, to peripheral tissues and organs. Angiotensin II activates the RAS via the angiotensin II type 1 receptor (AT1R), a GPCR expressed on cells within the cardiovascular system.

Although AT1R activation leads to stimulation of cardiac contractility, it simultaneously results in an increase in blood pressure and sodium and water retention in the kidney. As such, cardiac performance is maintained in the short term, but longer-term damage may be caused as the heart must pump against higher pressure (afterload) and is overstretched when filled (preload). As a result, while stimulation of AT1R is theoretically an attractive therapeutic goal, it results in the failing heart to pump less efficiently, possibly causing progressive damage to the muscular tissue of the heart, while fluid retention can lead to kidney damage.

Current AT1R-targeted therapies for chronic heart failure, angiotensin receptor blockers (ARBs), act as AT1R antagonists, blocking the effects of angiotensin II. Thus, while blood pressure is decreased and kidney function is preserved, cardiac contractility stimulation is prevented. Therefore, the utility of these drugs is limited for the treatment of AHF where there is the risk of acute impairment of cardiac function.

Through its work on the AT1R and its ABLE platform, Trevena has determined that cardiac contractility is primarily driven through the β-arrestin pathway when activating AT1R, while the effects on blood pressure and sodium and water retention are mediated through G-protein signaling. As such, the company has designed TRV027 as a β-arrestin biased ligand targeting AT1R. This rationally designed candidate is intended to improve cardiac contractility, while at the same time to not increase blood pressure or sodium/water retention.

Clinical development program

Trevena has completed three clinical trials of TRV027, including two Phase 1 trials and a Phase 2a study, as described below. In January 2014, the company initiated a Phase 2b study, which is expected to read out in 4Q15.

Phase 1 trials

Trevena conducted two Phase 1 trials for TRV027, a single-center, crossover trial in healthy subjects and a furosemide combination trial in heart failure patients with concomitant renal dysfunction. These trials support the pharmacokinetics/pharmacodynamics of the drug candidate, as well as its initial safety profile.

The first trial evaluated four-hour infusions of TRV027 in 20 healthy subjects at doses ranging from 0.01 to 20 µg/kg/min. The primary objective of the trial was to evaluate the tolerability and pharmacokinetics (PK) of TRV027 as a monotherapy. Results showed that TRV027 was well tolerated with no serious adverse events or clinically significant adverse events reported, even at doses up to 20 times higher than the expected therapeutic dose. The results also supported linear pharmacokinetics, and TRV027 was rapidly cleared when the infusion was stopped, which could support the ability to reverse any unexpected hypotensive effects that may occur in a clinical setting. There was no urinary excretion of TRV027 and thus, it is not expected that any dose adjustments would be required for renal insufficiency, which could facilitate the use of TRV027 in the emergency room setting. A sodium restriction sub-study demonstrated the ability of TRV027 to reduce load on the heart in patients with elevated RAS.

The second trial was a Phase 1b study (NCT01444872) intended to evaluate the pharmacokinetics and renal safety of TRV027 co-administered with furosemide in 17 patients with a history of moderate heart failure and concomitant renal dysfunction. Two cohorts of six subjects and one cohort of five subjects were enrolled in this two-period crossover trial. TRV027 was administered using a standard dosing paradigm, with doses of 1.25 mg/hr, 6.25 mg/hr, and 31.25 mg/hr (equivalent to 0.35 µg/kg/min, 1.74 µg/kg/min and 8.68 µg/kg/min, respectively, for a 60 kg person), without weight correction. The plasma concentrations obtained were similar to those obtained when TRV027 was administered on a per-kg basis to subjects with normal kidney function, suggesting that a standard dosing approach with no adjustment for weight or renal impairment is appropriate. This regimen would facilitate use in the emergency room where patients are not routinely weighed.

TRV027 was well-tolerated in these renally impaired subjects. There were no TRV027-related clinically significant or serious adverse events reported. Previously, reports have shown that oral furosemide administration produces a reduction in GFR that can be inhibited by blocking the effects of elevated angiotensin II. In this trial, however, there was no effect of the single dose of furosemide on GFR or RPF. Therefore, it was not possible to show a renal protective effect of TRV027. However, the trial did demonstrate that TRV027 itself preserved GFR and RPF, before and after furosemide administration. Moreover, co-administration of TRV027 did not impair furosemide's effect on diuresis or urinary sodium excretion.

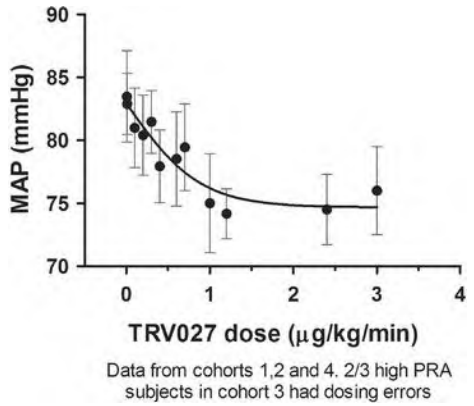
Complete Phase 2a trial

The completed Phase 2a trial was conducted to evaluate TRV027 in patients with advanced stable heart failure and to measure its effects on blood circulation (hemodynamics). Based on pre-clinical and Phase 1 data, the hemodynamic effects of TRV027 were expected to depend on elevation of RAS activity (i.e., the drug was expected to improve cardiac contractility in patients with an activated RAS). Therefore, the data were analyzed based on plasma renin activity (PRA) elevation, as PRA is an enzyme in the RAS cascade and serves as a measure of RAS activity. The trial enrolled 24 AHF patients and included a dose-ranging portion, evaluating 14 different doses across three dosing regimens, and a double-blind, placebo-controlled portion. The dosing regimens evaluated were: 1) 0.1 µg/kg/min titrated up to 1 µg/kg/min; 2) 0.3 µg/kg/min titrated up to 3 µg/kg/min; and 3) 1 µg/kg/min titrated up to 10 µg/kg/min.

Eleven of the 24 treated subjects had high PRA, defined as a level greater than 5.82 ng/ml/hr, which is the upper limit of normal. In these patients, TRV027 produced a dose-related decrease in mean arterial pressure (MAP), which was sustained during the steady state infusion (Figure 12). This decrease in MAP was reversed during the wash-out period following the end of the infusion. This reversal of effect was statistically significant compared to both placebo ($p>0.01$) and normal PRA subjects ($p>0.001$). The decrease in MAP in the high PRA subjects compared to subjects receiving placebo in the maintenance phase was also statistically significant ($p<0.05$).

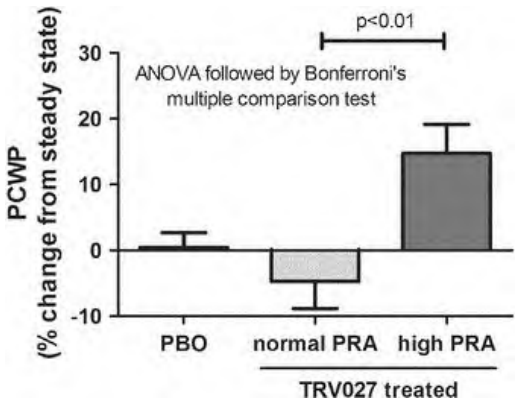
Evidence of pharmacologic effects on PCWP was observed in subjects with elevated PRA. PCWP dropped in subjects with high PRA during the titration phase, an effect that was sustained during the maintenance phase and reversed during the washout phase. The interpretation of the results in the titration and maintenance phases was complicated by a baseline drift in PCWP in the placebo group. However, the increase in PCWP when the TRV027 infusion was stopped was clear and statistically significant in high PRA subjects compared to normal PRA subjects ($p<0.01$; Figure 13).

FIGURE 12. Effect of TRV027 on Mean Arterial Pressure in Advanced Stable Heart Failure Subjects with Elevated PRA



Source: Company reports

FIGURE 13. Reversal of Effect of TRV027 on Pulmonary Capillary Wedge Pressure in Advanced Stable Heart Failure Subjects



Source: Company reports

Ongoing Phase 2b trial (BLAST-AHF)

In January 2014, Trevena initiated the BLAST-AHF Phase 2b trial (NCT01966601) investigating TRV027 in subjects with acute heart failure. The trial is a randomized, double-blind, standard-of-care-controlled study comparing TRV027 plus standard heart failure therapy to standard therapy alone. At least 500 patients are expected to be enrolled in BLAST-AHF and randomized to receive one of three doses of TRV027 (1.0 mg/hr, 5.0 mg/hr, and 25 mg/hr) or placebo, in addition to standard-of-care therapy. The study is enrolling patients with both low ejection fraction and preserved ejection fraction, since RAS elevation is a key component of both conditions. TRV027 or placebo will be initiated soon after presentation to the hospital, and then continue to be administered for a minimum of 48 hours and up to 96 hours. The primary endpoint of the trial is a composite of five clinically important outcomes: mortality, worsening heart failure, hospital readmission rate, dyspnea, and length of hospital stay.

An interim analysis is planned after 300 patients have been enrolled and, depending on the outcome of that analysis, enrollment into one or more of the TRV027 arms may be discontinued. Final top-line results are anticipated to read-out in 4Q15.

Commercial opportunity in heart failure

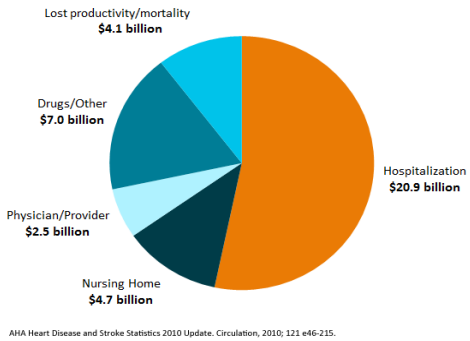
According to the American Heart Association (AHA), there are more than five million people in the U.S. with heart failure and it is projected that prevalence will increase by 46% from 2012 to 2030. There are 825,000 new cases of heart failure in the U.S. annually and the incidence increases to 10 per 1,000 population after 65 years of age. One in nine deaths in 2009 included heart failure as a contributing cause and in 2010, there were 280,000 deaths with heart failure as a contributing factor and 58,000 deaths with heart failure as the underlying condition.

Heart failure is one of the most common reasons for hospital admissions among those 65 years and older. According to the National Hospital Discharge Survey (NHDS) data, in 2010 in the U.S., there were over five million hospital discharges where heart failure was listed as a component of the diagnosis. More than 20% of these listed heart failure as the primary diagnosis. Per 2010, national hospital discharge statistics from 25 countries in Europe, it is estimated that there were a total of 1.6 million hospitalizations with a primary heart failure diagnosis in those countries.

The majority of subjects experiencing an AHF event have a worsening of existing chronic heart failure (CHF). Despite extended stays in the hospital, up to about 50% of AHF patients remain symptomatic upon discharge, according to data from ADHERE, a national U.S. registry of over 100,000 patients admitted to the hospital with AHF between 2000 and 2005. Further, the risk of readmission is 25% after 30 days and the one-year mortality rate is approximately 30%.

In all, heart failure causes a significant burden to the healthcare system. The AHA estimates that heart failure costs in the U.S. exceed $30bil annually, including the cost of health care services, medications to treat heart failure, and missed days of work (Figure 14). Additionally, the AHA estimates that the cost of heart failure hospitalization in the U.S. is in excess of $20bil.

FIGURE 14. Costs Associated with Heart Failure in the U.S.



Source: AHA Heart Disease and Stroke Statistics 2010 Update, Circulation, 2010; 121 e46-215; Company website

Current Treatment Options for AHF

Currently utilized therapeutic AHF treatment options are shown in Figure 15. The most frequently used class of drug for the treatment of AHF is loop diuretics, such as furosemide. These drugs are used as the first-line treatment in about 90% of AHF patients and facilitate excretion of excess fluid, providing relief of symptoms and improving tissue oxygenation. However, approximately half of AHF patients remain symptomatic upon hospital discharge. Moreover, aggressive diuresis can cause kidney dysfunction, which in AHF patients is associated with higher mortality and an increased risk of hospital readmission. Additionally, diuretic therapy has been shown to induce activation of RAS, which as described above capitulates the cycle of stress on the heart and kidney.

FIGURE 15. Currently Available AHF Treatment Options

Treatment class	Example(s)	Beneficial Effects	Negative Effects
Loop diuretics	furosemide	Remove excess fluid from kidneys	Can worsen renal function
Vasodilators	nitrates, nesiritide	Reduce blood pressure, reducing load on the heart	Hypotension, other agent-dependent effects
Inotropes	dobutamine	Reduce blood pressure, reducing load on the heart	increase mortality through an increased risk of arrhythmia

Source: Company reports

IV vasodilators, including nitroglycerin, nitroprusside, and nesiritide, are the second-most common treatment option for AHF. These drugs effectively reduce blood pressure; however, hypotension is the most common serious side effect. In addition, each agent is associated with undesirable side effects and other limitations. Nitroglycerin promotes the RAS response, and its use is further limited by rapid development of tolerance. Nitroprusside is associated with potential cyanide toxicity and cannot be used without intensive monitoring. Nesiritide effectively lowers blood pressure, but if it is lowered too far, the effect is difficult to reverse; prolonged hypotension may produce end-organ dysfunction. Moreover, nesiritide has been associated with worsening renal function and an increase in mortality.

Inotropes may be used in severe cases and those characterized by very low cardiac output. Inotropes increase cardiac contractility by mobilizing calcium but at the expense of increased oxygen consumption and risk of arrhythmia. While inotropes can improve symptoms in the short term, they have, to date, been demonstrated to increase mortality.

Developmental competitive landscape

Serelaxin: Novartis' serelaxin (RLX030) is an agonist of the relaxin receptor agonist, under regulatory review in both the U.S. and EU. Serelaxin is a form of human relaxin 2, a naturally occurring hormone present in both men and women, which rises in women during pregnancy to promote vasodilation and renal function. The therapy is thought to have multiple effects, including relaxing the blood vessels, reducing fluid buildup and protecting the heart and vital organs from the damaging effects of an AHF episode. The FDA's Cardiovascular and Renal Drugs Advisory Committee (CRDAC) was originally scheduled to discuss Novartis' BLA on February 13, 2014; however, the meeting was postponed due to weather conditions. In January 2014, following a negative opinion for serelaxin from the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA), Novartis announced it would file a resubmission package, with a revised opinion possible in 2Q14. The filings were based on the results of the RELAX-AHF Phase 3 study in addition to supportive Phase 2 data. The trial achieved one dyspnea endpoint (visual analog scale [VAS] to day five), while failing to show a benefit on the second (Likert scale to 24 hours). Serelaxin demonstrated a 47% reduction in worsening heart failure, a 37% reduction in cardiovascular mortality, and a 37% reduction in all-cause mortality. A second Phase 3 study (RELAX-AHF-2) was initiated in September 2013 with a primary endpoint of cardiovascular death.

Omecamtiv: Cytokinetics and partner Amgen are in Phase 2 development of omecamtiv mecarbil, a novel cardiac myosin activator, as a treatment for heart failure. The expansion phase of the Phase 2 COSMIC-HF trial is expected to begin in the near term, with results expected in 2015. Positive results from the ATOMIC-AHF Phase 2b trial, announced in September 2013, support the advancement of the program into Phase 3 development, in our view. While the trial was not powered to generate statistically significant results, dose-dependent improvements in dyspnea were observed. At the highest omecamtiv dose, the dyspnea response rate was 51% vs. 41% in the pooled placebo data (effect size: 23%; 95% CI: 0.97, 1.55). Additionally, there was a dose-dependent trend toward an improvement in heart failure worsening with omecamtiv. At the highest dose cohort, 9% of omecamtiv patients had worsening heart failure vs. 17% for the pooled placebo group.

Ularitide: Cardiorentis's ularitide, a chemically synthesized form of urodilatin, a natriuretic peptide produced in the kidneys, is in Phase 3 development as an intravenous (IV) infusion treatment for acute heart failure (AHF). Urodilatin induces excretion of sodium into the urine (natriuresis) and increased urine production (diuresis) to regulate fluid balance and sodium haemostasis. Ularitide induces natriuresis and diuresis by binding to specific natriuretic peptide receptors (NPR-A, NPR-B, and other natriuretic peptide receptors), thereby increasing intracellular cyclic guanosine monophosphate (cGMP) helping to relax smooth muscle tissues, leading to vasodilation and increased blood flow. In February 2014, Cardiorentis initiated the TRUE-AHF Phase 3 trial investigating whether early treatment with IV ularitide may reduce AHF symptoms in the short-term and cardiovascular mortality in the long-term, with cardiovascular mortality as a primary efficacy endpoint.

Potential for TRV027 to provide a differentiated treatment option

As summarized above, current treatment options have limitations and thus, a large unmet need exists for improved therapeutic approaches to treat AHF. Key aspects of a target therapeutic profile include the ability to improve blood circulation through vasodilation, facilitate fluid excretion by the kidneys, and enhance cardiac function. Based on results from the Phase 1 and Phase 2 trials completed to date, we believe TRV027 may address each of these criteria. In our view, the drug candidate may have the potential to reduce mortality rates, hospital readmission rates, and lengths of hospital stay, and therefore, may provide a novel and differentiated treatment for AHF in the hospital setting.

TRV027 has demonstrated benefits on the three key organ systems impacted by heart failure, the circulatory system, heart, and kidneys. TRV027 rapidly and reversibly lowered blood pressure and pulmonary capillary wedge pressure (PCWP), as demonstrated in the Phase 2a trial. As shown in the Phase 1b trial, it may be possible to co-administer TRV027 with furosemide. Further beneficial characteristics of TRV027 are self-limiting and rapidly resolvable blood pressure effects. In a Phase 2a clinical trial, there was a dose-dependent decrease in blood pressure up to doses of 1 µg/kg/min but no further reduction in blood pressure was seen at doses up to 3 µg/kg/min. This characteristic would offer a safety advantage over current vasodilators, which can cause hypotension. The short half-life of the drug could also enable avoidance of prolonged hypotension.

In our view, the emerging clinical profile of TRV027 supports the potential to improve symptoms and outcomes, such as hospital readmission rates, length of hospital stay, and mortality rates. We note that no currently approved therapies for AHF demonstrate benefit on long-term outcomes. As blockade of the RAS pathway has been shown to have morbidity and mortality benefits in chronic heart failure, and TRV027 enables biased activation of the β-arrestin pathway, it could be the first RAS therapy in the acute hospital setting, allowing improved blood circulation while mitigating risks of increased blood pressure and kidney damage.

TRV027 Revenue Model

We project revenues for TRV027 in both the U.S. (Figure 16) and Europe (Figure 17) in two settings, including primary and secondary heart failure discharges. Our assumptions are detailed below.

U.S. Revenue Projections for TRV027

In the U.S. in 2010 there were approximately one million primary and secondary hospital heart failure discharges each, and we estimate annual growth of 1.5% for both types. Of these discharged patients, we estimate throughout our forecast period that 90% of primary discharges and 20% of secondary discharges will be treated with a heart failure therapeutic. Of those, we estimate that 25% would be excluded from potential TRV027 treatment due to hypotension. For the addressable patient population, we forecast 2% penetration in 2018, ramping to 20% in 2024 and remaining flat thereafter. We estimate a daily cost of $800 beginning in 2018, increasing at a rate of 3%, with an average treatment duration of 2.5 days. According to these assumptions, we forecast 2026 gross U.S. sales of $531MM. We project a gross-to-net adjustment of 10% beginning in 2018 and ramping to 18% in 2026, yielding 2026 net revenues of $435MM. We forecast a royalty rate of 15% beginning in 2018 and increasing to 18% in 2023 and remaining flat thereafter. As a result, we project U.S. 2026 royalties to Trevena of $78MM.

FIGURE 16. TRV027 U.S. Revenue Model

U.S. TRV027 Revenue Model	2010	2011	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026
Primary HF Discharges	1,000,000	1,015,000	1,109,845	1,126,493	1,143,390	1,160,541	1,177,949	1,195,618	1,213,552	1,231,756	1,250,232	1,268,986
% growth		1.5%	1.5%	1.5%	1.5%	1.5%	1.5%	1.5%	1.5%	1.5%	1.5%	1.5%
Secondary HF Discharges	1,000,000	1,015,000	1,109,845	1,126,493	1,143,390	1,160,541	1,177,949	1,195,618	1,213,552	1,231,756	1,250,232	1,268,986
% growth		1.5%	1.5%	1.5%	1.5%	1.5%	1.5%	1.5%	1.5%	1.5%	1.5%	1.5%
Patients treated with a HF drug	1,100,000	1,116,500	1,220,829	1,239,142	1,257,729	1,276,595	1,295,744	1,315,180	1,334,908	1,354,931	1,375,255	1,395,884
Primary HF Discharges	900,000	913,500	998,860	1,013,843	1,029,051	1,044,487	1,060,154	1,076,056	1,092,197	1,108,580	1,125,209	1,142,087
% treated	90.0%	90.0%	90.0%	90.0%	90.0%	90.0%	90.0%	90.0%	90.0%	90.0%	90.0%	90.0%
Secondary HF Discharges	200,000	203,000	221,969	225,299	228,678	232,108	235,590	239,124	242,710	246,351	250,046	253,797
% treated	20.0%	20.0%	20.0%	20.0%	20.0%	20.0%	20.0%	20.0%	20.0%	20.0%	20.0%	20.0%
Addressable patient population	825,000	837,375	915,622	929,356	943,297	957,446	971,808	986,385	1,001,181	1,016,198	1,031,441	1,046,913
% excluded due to hypotension	25.0%	25.0%	25.0%	25.0%	25.0%	25.0%	25.0%	25.0%	25.0%	25.0%	25.0%	25.0%
Number of patients treated with TRV027				18,587	47,165	86,170	145,771	177,549	190,224	203,240	206,288	209,383
% penetration				***2.0%***	***5.0%***	***9.0%***	***15.0%***	***18.0%***	***19.0%***	***20.0%***	***20.0%***	***20.0%***
Treatment cost per patient				$2,000	$2,060	$2,122	$2,185	$2,251	$2,319	$2,388	$2,460	$2,534
Cost per day				$800.00	$824.00	$848.72	$874.18	$900.41	$927.42	$955.24	$983.90	$1,013.42
Annual price increase				0.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%
Avg. days of treatment				2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5
Gross sales ($MM)				**37.2**	**97.2**	**182.8**	**318.6**	**399.7**	**441.0**	**485.4**	**507.4**	**530.5**
Gross-to-net adjustment				10.0%	11.0%	12.0%	13.0%	14.0%	15.0%	16.0%	17.0%	18.0%
Net sales ($MM)				**33.5**	**86.5**	**160.9**	**277.2**	**343.7**	**374.9**	**407.7**	**421.2**	**435.0**
Royalty rate				15.0%	15.0%	15.0%	15.0%	15.0%	18.0%	18.0%	18.0%	18.0%
Royalties to Trevena ($MM)				**5.0**	**13.0**	**24.1**	**41.6**	**51.6**	**67.5**	**73.4**	**75.8**	**78.3**

Source: JMP Securities LLC, Company reports

EU Revenue Projections for TRV027

In the EU in 2010 there were approximately 1.6 million and 1.5 million primary and secondary hospital heart failure discharges, respectively, and we estimate annual growth of 1.5% for both types. Of these discharged patients, we estimate throughout our forecast period that 90% of primary discharges and 20% of secondary discharges will be treated with a heart failure therapeutic. Of those, we estimate that 25% would be excluded from potential TRV027 treatment due to hypotension. For the addressable patient population, we forecast 2% penetration in 2019, ramping to 18% in 2025 and remaining flat thereafter. We estimate a daily cost of $577 beginning in 2019, increasing at a rate of 3%, and an average treatment duration of 2.5 days. According to these assumptions, we forecast 2026 gross EU sales of $529MM. We project a gross-to-net adjustment of 11% beginning in 2019 and ramping to 18% in 2026, yielding 2026 net revenues of $434MM. We forecast a royalty rate of 12% beginning in 2019 and increasing to 16% in 2024 and remaining flat thereafter. As a result, we project 2026 EU royalties to Trevena of $69MM.

FIGURE 17. TRV027 EU Revenue Model

EU TRV027 Revenue Model	2010	2011	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026
Primary HF Discharges	1,600,000	1,624,000	1,775,752	1,802,388	1,829,424	1,856,865	1,884,718	1,912,989	1,941,684	1,970,809	2,000,371	2,030,377
% growth		1.5%	1.5%	1.5%	1.5%	1.5%	1.5%	1.5%	1.5%	1.5%	1.5%	1.5%
Secondary HF Discharges	1,500,000	1,522,500	1,664,767	1,689,739	1,715,085	1,740,811	1,766,923	1,793,427	1,820,329	1,847,634	1,875,348	1,903,478
% growth		1.5%	1.5%	1.5%	1.5%	1.5%	1.5%	1.5%	1.5%	1.5%	1.5%	1.5%
Patients treated with a HF drug	1,740,000	1,766,100	1,931,130	1,960,097	1,989,499	2,019,341	2,049,631	2,080,376	2,111,581	2,143,255	2,175,404	2,208,035
Primary HF Discharges	1,440,000	1,461,600	1,598,177	1,622,149	1,646,482	1,671,179	1,696,246	1,721,690	1,747,516	1,773,728	1,800,334	1,827,339
% treated	90.0%	90.0%	90.0%	90.0%	90.0%	90.0%	90.0%	90.0%	90.0%	90.0%	90.0%	90.0%
Secondary HF Discharges	300,000	304,500	332,953	337,948	343,017	348,162	353,385	358,685	364,066	369,527	375,070	380,696
% treated	20.0%	20.0%	20.0%	20.0%	20.0%	20.0%	20.0%	20.0%	20.0%	20.0%	20.0%	20.0%
Addressable patient population	1,305,000	1,324,575	1,448,348	1,470,073	1,492,124	1,514,506	1,537,223	1,560,282	1,583,686	1,607,441	1,631,553	1,656,026
% excluded due to hypotension	25.0%	25.0%	25.0%	25.0%	25.0%	25.0%	25.0%	25.0%	25.0%	25.0%	25.0%	25.0%
Number of patients treated with TRV027				0	29,842	60,580	122,978	218,439	253,390	273,265	293,680	298,085
% penetration				***0.0%***	***2.0%***	***4.0%***	***8.0%***	***14.0%***	***16.0%***	***17.0%***	***18.0%***	***18.0%***
Treatment cost per patient				$1,400	$1,442	$1,485	$1,530	$1,576	$1,623	$1,672	$1,722	$1,773
Cost per day				$560.00	$576.80	$594.10	$611.93	$630.28	$649.19	$668.67	$688.73	$709.39
Annual price increase				0.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%	3.0%
Avg. days of treatment				2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5	2.5
Gross sales ($MM)				**0.0**	**43.0**	**90.0**	**188.1**	**344.2**	**411.2**	**456.8**	**505.7**	**528.6**
Gross-to-net adjustment				10.0%	11.0%	12.0%	13.0%	14.0%	15.0%	16.0%	17.0%	18.0%
Net sales ($MM)				**0.0**	**38.3**	**79.2**	**163.7**	**296.0**	**349.6**	**383.7**	**419.7**	**433.5**
Royalty rate				12.0%	12.0%	12.0%	12.0%	12.0%	12.0%	16.0%	16.0%	16.0%
Royalties to Trevena ($MM)				**0.0**	**4.6**	**9.5**	**19.6**	**35.5**	**41.9**	**61.4**	**67.2**	**69.4**

Source: JMP Securities LLC, Company reports

We forecast TRV027 worldwide gross revenue in 2026 of $1.06bn, with net sales of $869MM, and royalties to Trevena of $148MM.

Forest option and license agreement

In May 2013, Trevena entered into option and license agreements with Forest Laboratories, under which the company granted Forest an exclusive option to license TRV027. Should Forest exercise the option, Forest would obtain an exclusive worldwide license to develop and commercialize TRV027 and specified related compounds. Forest would be responsible for subsequent development, regulatory approval, and commercialization of TRV027 including all costs. Forest may exercise its option at any time before Trevena delivers Phase 2b BLAST-AHF clinical trial results to Forest and during a specified period of time thereafter.

Under the terms of the agreement, Trevena would receive an upfront option exercise fee of $65MM and could be entitled to additional milestones totaling $365MM, as well as tiered royalties between 10% and 20% on net sales. Royalty rates on net sales in the U.S. would be somewhat higher than outside the U.S., although specific terms have not been disclosed.

Intellectual property

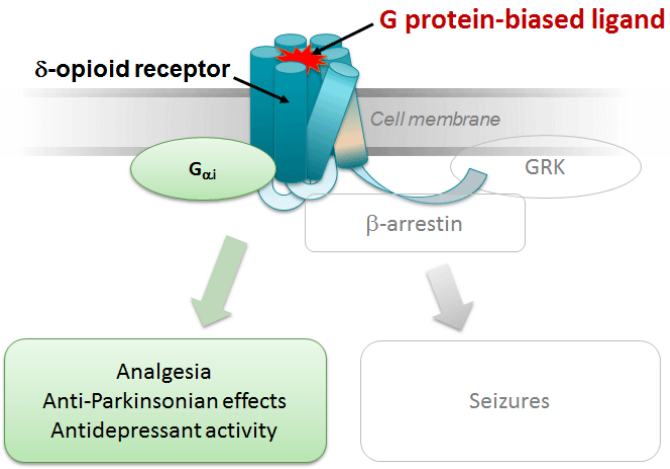
There is one issued U.S. patent for TRV027 (U.S. Patent No. 8,486,885), covering the drug candidate's composition of matter. This patent is expected to expire in 2031, excluding potential patent term extension. The TRV027 patent portfolio also includes two pending U.S. patent applications, which claim a genus of compounds that would cover TRV027 and methods of using TRV027. If issued, these patents would expire no earlier than 2029. Related patent applications have been filed in several other countries and are pending.

EARLY-STAGE PIPELINE

TRV734 - Oral μ-Opioid Biased Ligand for Moderate-to-Severe Pain

Trevena is developing TRV734, a small molecule G protein biased ligand at the μ-opioid receptor, as a first-line, orally administered compound for the treatment of moderate to severe acute and chronic pain. Like TRV130, TRV734 exploits a well-established mechanism of pain relief by targeting the μ-opioid receptor with enhanced selectivity for the signaling pathway that appears linked to analgesia as opposed to the β-arrestin signaling pathway associated with side effects (Figure 18). TRV734 may have an improved efficacy and side effect profile as compared to current commonly prescribed oral analgesics, such as oxycodone.

FIGURE 18. Hypothesized δ-opioid Receptor Agonist Proposed Mechanism of Action



Source: Company website

Pre-clinical data

TRV734 has similar in vitro and in vivo profiles compared to TRV130. It is highly selective for the μ-opioid receptor, where, like the most powerful opioid analgesics, it is a strong agonist of G protein coupling. TRV734 is distinct from those analgesics in its very weak recruitment of β-arrestins to the μ-opioid receptor. In Trevena's pre-clinical studies, TRV734 showed analgesic effects in pre-clinical pain models similar to oxycodone and morphine, causing less constipation compared to equivalently analgesic doses of oxycodone and morphine. Based on these data, TRV734 may have improved gastrointestinal tolerability in humans at analgesic doses that offer comparable analgesic effectiveness to current opioid therapies.

TRV734 is active after oral administration in mice and rats, and has high oral bioavailability and is well tolerated in non-human primates.

TRV734 Clinical Program

In February 2014, Trevena initiated a Phase 1 trial to evaluate the safety, tolerability, PK and PD of single-ascending doses of TRV734 in healthy subjects. The potentially efficacious dose range of TRV734 will also be evaluated using pupilometry, a validated biomarker for mu-opioid receptor engagement. The company anticipates the trial to conclude by the end of 3Q14, with data read-out by year-end 2014.

Development strategy

The company intends to seek a collaborator for TRV734 with experience in developing and commercializing controlled-substance therapeutics in chronic care pain markets, while retaining rights to commercialize TRV734 in hospital and specialist markets in the U.S.

TRV734 Intellectual property

Trevena's patent portfolio for TRV734 includes two pending U.S. patent applications claiming TRV734, other compounds and/or methods of making or using the same. If issued, the pending U.S. applications are predicted to expire no earlier than 2032, subject to any disclaimers or extensions. A related PCT application was filed and national patent applications have been filed in a number of other countries. Any patents resulting from these national patent applications, if issued, are predicted to expire no earlier than 2032, subject to any disclaimers or extensions.

δ-opioid Receptor Program

The company is developing orally bioavailable, small molecule G protein biased ligands of the δ-opioid receptor for the treatment of CNS disorders. The initial focus of the program is anticipated to be on Parkinson's disease, pain, or depression.

Pre-clinical data

Pre-clinical data are supportive of further efforts to target the δ-opioid receptor in order to develop treatments of CNS disorders, such as Parkinson's disease, pain, and depression. In the past, other approaches to modulate the δ-opioid receptor were limited by a significant risk of seizure associated with this target. However, Trevena has identified potent δ-opioid receptor ligands that demonstrate efficacy in animal models of depression, Parkinson's disease, and pain while avoiding inducing seizures through selective activation of the G protein receptor without engaging β-arrestin. In vivo data are further supported by data for δ-agonists in β-arrestin knockout mice, suggesting that β-arrestin plays a role in seizures. Trevena is conducting lead optimization and anticipates selecting a δ-opioid product candidate for further development in 1H14.

MANAGEMENT TEAM

Maxine Gowen, Ph.D. - President and CEO
Dr. Gowen is the founding President and CEO of Trevena. Prior to this Dr. Gowen held a variety of leadership roles at GlaxoSmithKline (GSK) over a period of fifteen years. Dr. Gowen was previously President and Managing Partner at SR One, the venture capital subsidiary of GSK, where she led its investments in and served on the board of directors of numerous companies. Until 2002, Dr. Gowen was Vice President, Drug Discovery, Musculoskeletal Diseases at GSK, responsible for drug discovery and early development for osteoporosis, arthritis, and metastatic bone disease. Dr. Gowen held a tenured academic position in the School of Pharmacology, University of Bath, UK from 1989-1992. She has authored more than 100 refereed scientific publications.

Dr. Gowen graduated with a B.Sc. in biochemistry from the University of Bristol, UK, received a Ph.D. in cell biology from the University of Sheffield, UK, and received an MBA from the Wharton School of the University of Pennsylvania. Dr. Gowen served on the Board of Directors of Human Genome Sciences (HGSI) until its acquisition by GSK in July 2012 and she is currently on the Board of Directors of the biotechnology industry association, BIO.

Michael W. Lark, Ph.D. - CSO and Senior Vice President, Research
Dr. Lark joined Trevena as Senior VP and Head of Research in February 2008. Prior to this, he was Vice President of Biology at Centocor R&D where he was responsible for the therapeutic discovery strategy and execution in immunology, oncology, tissue remodeling, and biomarkers. In this role, Dr. Lark managed a portfolio of approximately 15 drug discovery projects as well as supporting the development of 14 new molecular entities (two in late-stage clinical development) and one product. He was previously Director of Musculoskeletal Diseases at GlaxoSmithKline, where he managed a portfolio of drug discovery projects targeting osteoporosis, osteoarthritis, rheumatoid arthritis, and psoriasis. Before joining SmithKline Beecham in 1996, Dr. Lark was a Senior Investigator at Merck Research laboratories, where he led a drug discovery team targeting matrix metalloproteinase-3 for the treatment of osteoarthritis. He has published over 115 peer-reviewed papers, reviews, and book chapters. Dr. Lark received his B.S. in Microbiology from the Pennsylvania State University and his Ph.D. in Molecular Biology and Microbiology from the Case Western Reserve University Medical School. He completed a postdoctoral fellowship in the Department of Pathology at The University of Washington.

Roberto Cuca - Chief Financial Officer
Mr. Cuca joined Trevena as Senior Vice President and Chief Financial Officer in September 2013. Prior to joining, he held various leadership positions in the finance organization of Endo Health Solutions Inc. from March 2010 to August 2013, including, most recently, Treasurer and Senior Vice President, Finance. Prior to that, he was Director, Corporate and Business Development, at moksha8 Pharmaceuticals, Inc., an emerging markets-focused pharmaceutical company, from March 2008 until February 2010. From 2005 until 2008, he worked at JPMorgan Chase & Co. as an equity analyst covering U.S. pharmaceutical companies. Mr. Cuca received an M.B.A. from the Wharton School of The University of Pennsylvania, a J.D. from Cornell Law School, an A.B. from Princeton University and is a CFA charterholder.

David Soergel, M.D. - Senior Vice President, Clinical Development

Dr. Soergel joined Trevena in November 2009. Previously, he was Senior Director, Clinical Development at Concert Pharmaceuticals where he was responsible for clinical strategy and operations across diverse therapy areas, including infectious diseases and diabetic nephropathy. Prior to Concert, Dr. Soergel was Director of Discovery Medicine at GSK in the Cardiovascular/Urogenital Center of Excellence for Drug Discovery where he was responsible for leading compounds from the bench to the bedside in the areas of women's health and urology. At GSK, he served on multiple interdisciplinary working groups, including the Internal Cardiac Safety Panel and Pediatric Network. After completing an NIH-funded, post-doctoral fellowship and receiving the Fellow's Award for Basic Research from the Society for Pediatric Research, Dr. Soergel completed his clinical training in Pediatric Cardiology at Johns Hopkins Hospital. He underwent additional training in Heart Failure and Transplant at the Children's Hospital of Philadelphia.

Source: Company website

FIGURE 19. Trevena Earnings Model ($MM, except per share data)

(in thousands 000's)	2011	2012	2013E	1Q:14E	2Q:14E	3Q:14E	4Q:14E	2014E	1Q:15E	2Q:15E	3Q:15E	4Q:15E	2015E	2016E
Revenue														
TRV027			0	0	0	0	0	0	0	0	0	0	0	0.0
TRV130			0	0	0	0	0	0	0	0	0	0	0	0.0
Grant revenue	2,421	408	113	0	0	0	0	0	0	0	0	0	0	0.0
Collaboration revenue	0	400	67	0	0	0	0	0	0	0	0	0	0	0.0
Total Revenues	**2,421.4**	**808**	**180**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**
COGS		0	0	0	0	0	0	0	0	0	0	0	0	0
Gross Profit	**2,421.4**	**808**	**180**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**	**0**
Operating expenses														
R&D	15,109	13,295	16,240	7,500	12,000	16,000	16,000	51,500	16,000	16,000	12,000	8,000	52,000	54,600
SG&A	3,063	3,123	3,793	979	1,008	1,038	1,069	4,094	1,176	1,294	1,423	1,565	5,459	6,277
Total operating expenses	**18,172**	**16,418**	**20,033**	**8,479**	**13,008**	**17,038**	**17,069**	**55,594**	**17,176**	**17,294**	**13,423**	**9,565**	**57,459**	**60,877**
Operating income (loss)	**(15,750)**	**(15,610)**	**(19,853)**	**(8,479)**	**(13,008)**	**(17,038)**	**(17,069)**	**(55,594)**	**(17,176)**	**(17,294)**	**(13,423)**	**(9,565)**	**(57,459)**	**(60,877)**
Operating margin														
Other income (expense)	(60)	(26)	(1,448)	0	0	0	0	0	0	0	0	0	0	0
Change in fair value of warrant liability	11	45	(1,250)	0	0	0	0	0	0	0	0	0	0	0
Miscellaneous income	0	123	1	0	0	0	0	0	0	0	0	0	0	0
Interest income	4	1	0	0	0	0	0	0	0	0	0	0	0	0
Interest expense	(74)	(194)	(199)	0	0	0	0	0	0	0	0	0	0	0
Pretax income (loss)	**(15,810)**	**(15,636)**	**(21,301)**	**(8,479)**	**(13,008)**	**(17,038)**	**(17,069)**	**(55,594)**	**(17,176)**	**(17,294)**	**(13,423)**	**(9,565)**	**(57,459)**	**(60,877)**
Income tax	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Tax rate														
Net income (loss) to common	**(15,810)**	**(15,636)**	**(21,301)**	**(8,479)**	**(13,008)**	**(17,038)**	**(17,069)**	**(55,594)**	**(17,176)**	**(17,294)**	**(13,423)**	**(9,565)**	**(57,459)**	**(60,877)**
Accretion of preferred stock	(74)	(317)	-331	0	0	0	0	0	0	0	0	0	0	0
Net income (loss)	**(15,884)**	**(15,952)**	**(21,632)**	**(8,479)**	**(13,008)**	**(17,038)**	**(17,069)**	**(55,594)**	**(17,176)**	**(17,294)**	**(13,423)**	**(9,565)**	**(57,459)**	**(60,877)**
Net margin														
EPS														
Basic	**($27.27)**	**($23.70)**	**($28.96)**	**($0.33)**	**($0.50)**	**($0.66)**	**($0.65)**	**($2.14)**	**($0.65)**	**($0.66)**	**($0.51)**	**($0.36)**	**($2.17)**	**($2.24)**
Diluted	**($27.27)**	**($23.70)**	**($28.96)**	**($0.33)**	**($0.50)**	**($0.66)**	**($0.65)**	**($2.14)**	**($0.65)**	**($0.66)**	**($0.51)**	**($0.36)**	**($2.17)**	**($2.24)**
Shares outstanding														
Basic	582	673	747	25,734	25,863	25,992	26,122	25,928	26,253	26,384	26,516	26,649	26,450	27,182
% change		*15.6%*	*11.0%*	*3332.5%*	*0.5%*	*0.5%*	*0.5%*	*3371.3%*	*0.5%*	*0.5%*	*0.5%*	*0.5%*	*2.0%*	*2.0%*
Diluted	582	673	747	25,734	25,863	25,992	26,122	25,928	26,253	26,384	26,516	26,649	26,450	27,182
% change		*15.6%*	*11.0%*	*3332.5%*	*0.5%*	*0.5%*	*0.5%*	*3371.3%*	*0.5%*	*0.5%*	*0.5%*	*0.5%*	*2.0%*	*2.0%*
Cash Flow														
Net Income to common	(15,810)	(15,636)	(21,301)	(8,479)	(13,008)	(17,038)	(17,069)	(55,594)	(17,176)	(17,294)	(13,423)	(9,565)	(57,459)	(60,877)
Depreciation and amortization	802	788	727	180	180	180	180	720	180	180	180	180	720	720
Stock-based compensation	181	176	670	170	170	170	170	680	170	170	170	170	680	680
Other adjustments	1,546	(133)	1,612	0	0	0	0	0	0	0	0	0	0	1
Operating burn	**(13,282)**	**(14,805)**	**(18,292)**	**(8,129)**	**(12,658)**	**(16,688)**	**(16,719)**	**(54,194)**	**(16,826)**	**(16,944)**	**(13,073)**	**(9,215)**	**(56,059)**	**(59,476)**
Cash at start of period				55,000	106,872	94,214	77,526	55,000	60,806	43,980	27,036	13,963	60,806	4,748
Cash from operations				(8,129)	(12,658)	(16,688)	(16,719)	(54,194)	(16,826)	(16,944)	(13,073)	(9,215)	(56,059)	(59,476)
Cash from investing				0	0	0	0	0	0	0	0	0	0	0
Cash from financing				60,000	0	0	0	60,000	0	0	0	0	0	86,400
Shares issued				9,250				9,250					0	5,000
Price per share								0					0	18.00
Effect of FX				0	0	0	0	0	0	0	0	0	0	0
Cash at end of period			**55,000**	**106,872**	**94,214**	**77,526**	**60,806**	**60,806**	**43,980**	**27,036**	**13,963**	**4,748**	**4,748**	**31,671**
Investment securities			0	0	0	0	0	0	0	0	0	0	0	0
Cash and investment securities			**55,000**	**106,872**	**94,214**	**77,526**	**60,806**	**60,806**	**43,980**	**27,036**	**13,963**	**4,748**	**4,748**	**31,671**

Source: Company reports, JMP Securities

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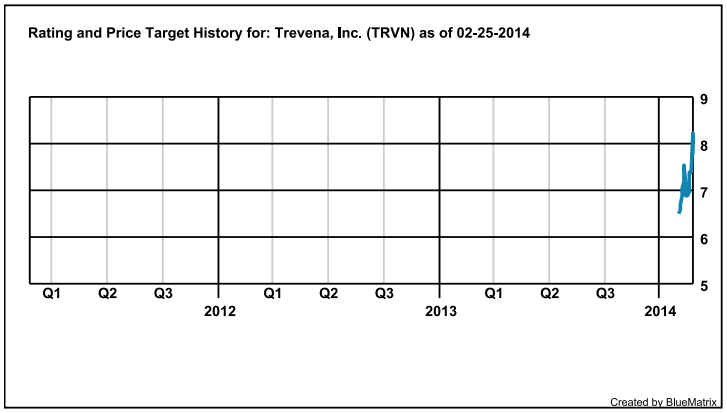
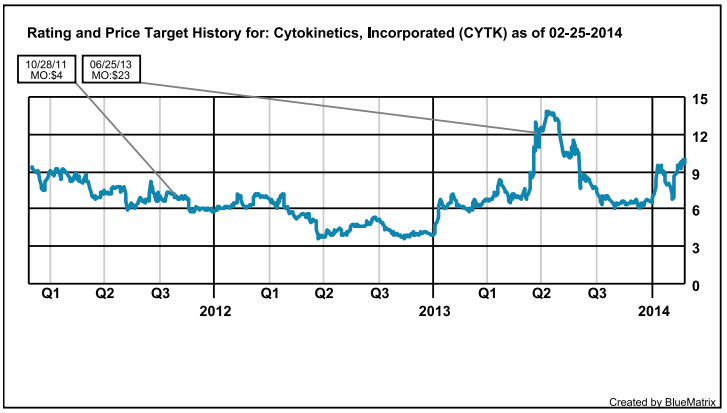
MARKET PERFORM	Hold	138	*32.09%*	Hold	138	*32.09%*	21	*15.22%*
MARKET UNDERPERFORM	Sell	8	*1.86%*	Sell	8	*1.86%*	0	*0%*
COVERAGE IN TRANSITION		43	*10.00%*		43	*10.00%*	0	*0%*
TOTAL:		430	*100%*		430	*100%*	111	*25.81%*

Stock Price Chart of Rating and Target Price Changes:

Note: First annotation denotes initiation of coverage or 3 years, whichever is shorter. If no target price is listed, then the target price is N/A. In accordance with NASD Rule 2711, the chart(s) below reflect(s) price range and any changes to the rating or price target as of the end of the most recent calendar quarter. The action reflected in this note is not annotated in the stock price chart. Source: JMP Securities.





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