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Results of Phase 1b Clinical Trial Comparing Trevena's TRV130 to Morphine Published in the Journal Pain

KING OF PRUSSIA, Pa.--(BUSINESS WIRE)-- Trevena, Inc. (NASDAQ: TRVN), a clinical stage biopharmaceutical company and the leader in the discovery of G protein coupled receptor (GPCR) biased ligands, today announced the publication of its Phase 1b data for TRV130 in the journal *Pain*. The manuscript, entitled "Biased agonism of the mu opioid receptor by TRV130 increases analgesia and reduces on-target adverse effects versus morphine: a randomized, double-blind placebo-controlled crossover study in healthy volunteers," can be viewed online at the *Pain* website, http://www.painjournalonline.com/.

"The strong analgesic efficacy of opioids comes with frequent and significant adverse effects and, to date, it has not been possible to separate these adverse effects from effective analgesia, making it challenging for physicians to adequately treat patients' pain," said Lynn Webster MD, of PRA Health Sciences, immediate past president of the American Academy of Pain Medicine and primary investigator on the study. "These data suggest that TRV130 may reduce patients' pain more effectively, act more quickly, produce less severe GI side effects and reduce the risk of respiratory depression compared to existing opioids, resulting in an improved margin of safety for dosing."

"The publication of these Phase 1b data in this leading peer-reviewed journal reflects the importance of the study and underscores the need for new pain therapies that offer an improved therapeutic window," stated Maxine Gowen, Ph.D., chief executive officer of Trevena. "We are building on these data in our ongoing Phase 2a/b trial, which is evaluating TRV130 versus morphine in patients following bunionectomy surgery. We expect top-line data from this trial in the first quarter of 2015."

The printed manuscript will appear in a future print issue of the journal. David G. Soergel, M.D., Trevena's senior vice president of clinical development, Franck Skobieranda M.D., Trevena's vice president of clinical development, and Michael W. Lark, Ph.D., Trevena's chief scientific officer and senior vice president of research were among the publication's authors.

About the TRV130 Phase 1b clinical trial

Trevena is developing TRV130, a small molecule G protein biased ligand at the mu-opioid receptor, as a first-line treatment for patients experiencing moderate to severe acute pain where intravenous administration is preferred. The *Pain* manuscript describes a randomized, double-blind, placebo-controlled, 5-period crossover study that enrolled 30 healthy adult males. Subjects were administered one of five treatments in each period: 1.5 mg, 3.0 mg, or 4.5 mg of TRV130 via intravenous administration, 10 mg morphine or placebo. The objectives of the trial were to evaluate the safety and tolerability of TRV130, evaluate the

analgesic effects of TRV130 versus placebo and versus morphine using the cold pain test, evaluate the effects of TRV130 versus placebo and versus morphine on respiratory drive, as measured by the ventilatory response to hypercapnia, evaluate the pharmacokinetics of TRV130, and evaluate subjective effects of TRV130 using a drug effects questionnaire.

As previously reported, TRV130 was analgesic in the cold pain test versus placebo at all three doses. Compared to 10 mg morphine, TRV130 at 3 mg and 4.5 mg showed increased analgesia with a more rapid onset of action, superior analgesic effect, and similar duration of action. In addition, at the 3 mg and 4.5 mg doses of TRV130, more subjects doubled baseline cold pain test latency and achieved maximum cold pain test latency of 180 seconds. In addition, TRV130, at doses with increased analgesia, produced less reduction in respiratory drive than morphine, as measured by ventilatory response to hypercapnia, less vomiting, and less severe nausea. Summary results were previously presented at the 2014 American Pain Society annual meeting.

About TRV130 and Acute Pain

The mu-opioid receptor is a well-established target for analgesics such as fentanyl and morphine, which are unbiased mu-opioid agonists. TRV130 activates the mu-opioid G protein pathway, which is associated with analgesia, and inhibits the beta-arrestin pathway, which, in preclinical studies, was associated with respiratory depression and constipation. The preclinical pharmacology of this novel molecule has been previously published in the *Journal of Pharmacology and Experimental Therapeutics*, with data suggesting that TRV130 is powerfully analgesic with an improved safety and tolerability profile when compared directly to classical opioids such as morphine. In the first clinical study of TRV130, which was published in the *Journal of Clinical Pharmacology* in March of 2014, TRV130 had robust CNS activity and was well tolerated in healthy volunteers.

Trevena anticipates that the initial market opportunity for TRV130 will be in the acute care hospital setting, with a focus on postoperative pain. Dosing of mu-opioid agonists, the most effective class of analgesics currently available, is limited by severe side effects such as respiratory depression, nausea and vomiting, constipation, and postoperative ileus, with the result that approximately 50% of surgical patients report moderate or severe pain while in the hospital despite the use of opioid analgesics. Trevena believes that TRV130 may offer improved analgesia with reduced incidence and severity of these on-target adverse effects, which could help ease the suffering and burden of care for post-surgical pain, as well as the financial impact of opioid-related adverse effects in US hospitals which is estimated to be up to $5 billion annually.

About Trevena

Trevena, Inc. is a clinical stage biopharmaceutical company that discovers, develops and intends to commercialize therapeutics that use a novel approach to target G protein coupled receptors, or GPCRs. Using its proprietary product platform, Trevena has identified and advanced three differentiated biased ligand product candidates into the clinic – TRV027 to treat acute heart failure, TRV130 to treat moderate-to-severe acute pain intravenously, and TRV734 to treat moderate-to-severe acute and chronic pain orally. Trevena also is advancing additional product candidates in its portfolio, including a preclinical program focused on central nervous system indications.

Cautionary Note on Forward Looking Statements

Any statements in this press release about future expectations, plans and prospects for the Company, including statements about the Company's strategy, its future operations, clinical development of its therapeutic candidates, its plans for potential future product candidates and other statements containing the words "anticipate," "believe," estimate," "expect," "intend," "may," "plan," "predict," "project," "target," "potential," "will," "would," "could," "should," "continue," and similar expressions, constitute forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995. Actual results may differ materially from those indicated by such forward-looking statements as a result of various important factors, including: the status, timing, cost and results of the Company's clinical trials, including the Phase 1b results and the timing of top-line data for the Phase 2a/b trial of TRV130; the uncertainties inherent in conducting future clinical trials; whether interim results from a clinical trial will be predictive of the final results of the trial or results of early clinical trials will be indicative of the results of future trials including with respect to the Phase 1b results for TRV130; expectations for regulatory approvals; availability of funding sufficient for the Company's foreseeable and unforeseeable operating expenses and capital expenditure requirements; other matters that could affect the availability or commercial potential of the Company's therapeutic candidates including TRV130, and other factors discussed in the Risk Factors set forth in the Company's Annual Report on Form 10-K and Quarterly Reports on Form 10-Q filed with the Securities and Exchange Commission (SEC) and in other filings the Company makes with the SEC from time to time. In addition, the forward-looking statements included in this press release represent the Company's views only as of the date hereof. The Company anticipates that subsequent events and developments may cause the Company's views to change. However, while the Company may elect to update these forward-looking statements at some point in the future, the Company specifically disclaims any obligation to do so, except as may be required by law.

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