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Avenue Therapeutics Announces Positive Topline Phase 3 Data for Intravenous Tramadol in the Management of Postoperative Pain

IV tramadol achieved primary and key secondary endpoints, as well as a clear dose response

Initiation of second pivotal Phase 3 trial planned for third quarter of 2018

Management to host conference call today at 8:30 a.m. EDT

NEW YORK, May 21, 2018 (GLOBE NEWSWIRE) -- Avenue Therapeutics, Inc. (NASDAQ:ATXI) ("Avenue"), a company focused on the development and commercialization of intravenous (IV) tramadol, today announced that its first pivotal Phase 3 trial of IV tramadol achieved the primary endpoint of a statistically significant improvement in Sum of Pain Intensity Difference over 48 hours (SPID48) compared to placebo in patients with moderate to moderately severe postoperative pain following bunionectomy surgery. In addition, the trial met its key secondary endpoints and demonstrated a clear dose response. Avenue plans to initiate a second pivotal Phase 3 trial of IV tramadol in patients following abdominoplasty surgery in the third quarter of 2018.

"There is a clear need for new therapies in the postoperative pain setting, where patients are often treated with Schedule II narcotics due to a lack of other options," said Harold Minkowitz, M.D., an investigator in IV tramadol's Phase 3 program. "IV tramadol, which acts by a dual mechanism, is widely used outside the U.S. in the postoperative setting. These Phase 3 results demonstrate that IV tramadol is well tolerated and rapidly and effectively induces pain relief in patients following bunionectomy surgery, a generally painful procedure, and suggest that IV tramadol could be an important new therapy for managing postoperative pain in our patients."

"We are greatly encouraged by the strong safety and efficacy results from our first Phase 3 trial, which support IV tramadol's potential to provide an improved IV treatment option for postsurgical pain, and to fill a significant gap between IV NSAIDs and Schedule II opioids," said Scott Reines, M.D., Ph.D., Avenue's Chief Medical Officer. "Moreover, the trial clearly defined the 50 mg dose that will be applied in our second Phase 3 trial in patients following abdominoplasty surgery as well as in our ongoing safety trial."

"IV tramadol has the potential to provide a convenient bridge to the widely prescribed oral tramadol. This combination could displace Schedule II narcotics altogether for many patients, and provide a treatment option with less potential for abuse and a lower risk of dependence," said Lucy Lu, M.D., Avenue's President and Chief Executive Officer. "We are

excited about these results and look forward to initiating a second pivotal Phase 3 trial in the third quarter and, assuming positive data from that study and our ongoing safety trial, we anticipate filing an NDA with the U.S. Food and Drug Administration in late 2019."

Phase 3 Trial Design and Results

The Phase 3, multicenter, double-blind, placebo-controlled trial evaluated the efficacy and safety of IV tramadol in 409 patients following bunionectomy surgery. Patients were randomized in a 1:1:1 ratio to a postoperative regimen of 50 mg of IV tramadol, 25 mg of IV tramadol or placebo administered over 15 minutes at hours 0, 2, 4 and once every 4 hours thereafter, for up to 13 doses. Based on a previous pharmacokinetic study, the 50 mg dosing regimen produces a similar Cmax (peak serum concentration) and AUC (area under the curve) to those of 100 mg oral tramadol given every 6 hours at steady state and reaches such Cmax after the third dose at hour 4.

The primary endpoint of the bunionectomy study assessed the analgesic efficacy of IV tramadol compared to placebo as measured by SPID48. The key secondary endpoints included SPID24, total consumption of rescue medicine and Patient Global Assessment, which captures patients' perception of the treatment.

The IV tramadol 50 mg treatment arm achieved the primary endpoint of statistically superior improvement in SPID48 ($p=0.005$) compared to placebo. The 50 mg arm also met all three key secondary endpoints ($p < 0.01$). The profile of pain intensity over time demonstrated that IV tramadol 50 mg achieved statistically significant improvement in pain reduction as early as ½ hour (the first assessment timepoint) after dosing. The IV tramadol 25 mg treatment arm generally displayed intermediate results that fell between the 50 mg and the placebo arms, with a dose response observed across each of the primary and key secondary efficacy endpoints.

IV tramadol was well-tolerated with no reports of drug-related serious adverse events in the trial. One patient in the 50 mg IV tramadol arm discontinued the trial due to an adverse event (vomiting). The most common (≥5%) adverse events in the trial where IV tramadol 50 mg differed from placebo were nausea, vomiting, dizziness and somnolence. However, most of these adverse events were mild or moderate (Grade 1 or 2) with only 4 (3%) patients experiencing a Grade 3 event (vomiting) and no Grade 4 events in the IV tramadol 50 mg group. The overall safety profile of the IV tramadol 50 mg arm is consistent with known tramadol pharmacology and in this trial appeared to have a better tolerability profile than historical data of IV opioids in similar settings, which will be explored in Avenue's next Phase 3 trial.

Detailed trial results will be submitted for presentation at a future scientific conference or for publication in a journal.

Conference Call and Webcast

Avenue will host a conference call and webcast at 8:30 a.m. EDT today to discuss the topline Phase 3 data. To participate in the conference call, please dial (877) 273-6095 (domestic) or (647) 689-5538 (international) and enter the conference code: 2999651. A live audio webcast will be available on the Events page of the Investors section of Avenue's website at www.avenuetx.com. A replay of the audio webcast will be available approximately one hour after the call on the Events page of the Investors section of Avenue's website for a

period of 30 days following the call.

About IV Tramadol
Tramadol is a synthetic, dual-acting opioid with a unique mechanism of action that delivers opioid efficacy with less potential for abuse and a lower risk of dependence than conventional narcotics. Oral tramadol has a well-established efficacy and safety profile, and is currently approved and marketed in the U.S. for moderate to moderately severe pain in adults. There is currently no approved IV formulation in the U.S.

Avenue is evaluating IV tramadol in a pivotal Phase 3 clinical program: a trial in patients following bunionectomy surgery (NCT03290378) has been completed and a safety study (NCT03395808) is ongoing. A pivotal Phase 3 trial in patients following abdominoplasty surgery is expected to initiate in the third quarter of 2018.

About Avenue Therapeutics
Avenue Therapeutics, Inc. ("Avenue"), a Fortress Biotech (NASDAQ:FBIO) Company, is a specialty pharmaceutical company focused on the development and commercialization of intravenous (IV) tramadol for the management of moderate to moderately severe postoperative pain. IV tramadol may fill a gap in the acute pain market between IV acetaminophen/NSAIDs and IV conventional narcotics. Avenue is currently evaluating IV tramadol in a pivotal Phase 3 program for the management of postoperative pain. Avenue is headquartered in New York City. For more information, visit www.avenuetx.com.

About Fortress Biotech
Fortress Biotech, Inc. ("Fortress") is a biopharmaceutical company dedicated to acquiring, developing and commercializing novel pharmaceutical and biotechnology products. Fortress develops and commercializes products both within Fortress and through certain of its subsidiary companies, also known as Fortress Companies. In addition to its internal development programs, Fortress leverages its biopharmaceutical business expertise and drug development capabilities and provides funding and management services to help the Fortress Companies achieve their goals. Fortress and the Fortress Companies may seek licensings, acquisitions, partnerships, joint ventures and/or public and private financings to accelerate and provide additional funding to support their research and development programs. For more information, visit www.fortressbiotech.com.

Forward-Looking Statements
This press release may contain "forward-looking statements" within the meaning of Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934, each as amended. Such statements include, but are not limited to, any statements relating to our growth strategy and product development programs and any other statements that are not historical facts. Forward-looking statements are based on management's current expectations and are subject to risks and uncertainties that could negatively affect our business, operating results, financial condition and stock value. Factors that could cause actual results to differ materially from those currently anticipated include: risks relating to our growth strategy; risks relating to the results of research and development activities; risks relating to the timing of starting and completing clinical trials; our ability to obtain, perform under and maintain financing and strategic agreements and relationships; uncertainties relating to preclinical and clinical testing; our dependence on third-party suppliers; our ability to attract, integrate and retain key personnel; the early stage of products under development; our need for substantial additional funds; government regulation; patent and intellectual

property matters; competition; as well as other risks described in our SEC filings. We expressly disclaim any obligation or undertaking to release publicly any updates or revisions to any forward-looking statements contained herein to reflect any change in our expectations or any changes in events, conditions or circumstances on which any such statement is based, except as required by law.

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