Otonomy Reports Positive Top-Line Results from Phase 1/2 Clinical Trial of OTO-413 in Patients with Hearing Loss

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- *OTO-413 demonstrated a higher proportion of responders than placebo based on multiple speech-in-noise hearing tests*
- *A single intratympanic injection of OTO-413 was well-tolerated*
- *Otonomy intends to continue clinical development of OTO-413*
- *Management will review results during a conference call today at 8 a.m. ET*

SAN DIEGO, Dec. 17, 2020 (GLOBE NEWSWIRE) -- Otonomy, Inc. (Nasdaq: OTIC), a biopharmaceutical company dedicated to the development of innovative therapeutics for neurotology, today announced positive top-line results from the Phase 1/2 clinical trial of OTO-413 in subjects with speech-in-noise hearing difficulty. The randomized, double-blind, placebo-controlled trial demonstrated that a single intratympanic injection of OTO-413, a sustained exposure formulation of brain-derived neurotrophic factor (BDNF), was well-tolerated across all dose cohorts. Furthermore, there was demonstration of therapeutic activity of OTO-413 versus placebo across multiple clinically-validated speech-in-noise hearing tests at consecutive time points (Days 57 and 85). Based on these results, the company plans to continue development of OTO-413 for the treatment of hearing loss.

Assessment of OTO-413 Therapeutic Activity

All subjects enrolled in this trial self-reported hearing difficulty in a noisy environment that was confirmed by speech-in-noise (SIN) testing. Subjects could also have up to moderately-severe hearing loss by standard testing in a quiet background. Multiple clinically-validated SIN hearing tests including Digits-in-Noise (DIN), Words-in-Noise (WIN), and American English Matrix test were administered at baseline and following treatment at Day 15, 29, 57, and 85. The assessment of therapeutic activity is based on demonstration of a clinically meaningful improvement from baseline according to the thresholds utilized for each of the SIN tests. The top-line results below include the 9 subjects from the OTO-413 high dose (0.3 mg) cohort with test results on both Day 57 and Day 85 and 8 placebo subjects pooled from the last 3 dose cohorts.

- 6 out of 9 (67%) OTO-413 subjects demonstrated a clinically-meaningful improvement on at least one of the three SIN tests at both Days 57 and 85 versus 0 out of 8 (0%) for placebo.
- 3 out of 9 (33%) OTO-413 subjects demonstrated a clinically-meaningful improvement by two or more different SIN tests at both Days 57 and 85 versus 0 out of 8 (0%) for placebo.
- Considering the American English Matrix test that mimics a real world setting by using short sentences in background noise, 4 out of 9 (44%) OTO-413 subjects showed a clinically-meaningful improvement at both Days 57 and 85 compared to 0 out of 7 (0%) placebo subjects showing a clinically-meaningful improvement at any single time point.
- Most of the patients enrolled in this trial also had moderately-severe hearing loss by standard testing in a quiet background. The responder rate for OTO-413 was equally favorable in this subset with 5 out of 7 (71%) OTO-413 subjects demonstrating a clinically-meaningful improvement in at least one SIN test and 3 out of 7 (43%) responding by two or more tests at both Days 57 and 85 compared to 0 out of 6 (0%) placebo subjects.
- Improvements from baseline were also observed for multiple other exploratory endpoints and for OTO-413 treated subjects in the lower dose cohorts.

In summary, Otonomy believes that these higher responder rates for OTO-413 compared to placebo at two consecutive time points across multiple SIN tests demonstrates therapeutic activity and supports continued development of OTO-413 for the treatment of hearing loss.

OTO-413 Safety Evaluation

A total of 29 subjects were treated with OTO-413 across four ascending dose cohorts (0.01 mg, 0.03 mg, 0.10 mg and 0.30 mg) with a similar frequency of adverse events (AEs) reported as for placebo subjects. There was no apparent impact of OTO-413 dose on AE incidence, no serious AEs reported and no patients who discontinued the trial due to an AE. Otonomy believes these results demonstrate that a single intratympanic injection of OTO-413 was well-tolerated.

“Difficulty hearing a conversation with noise in the background is a common complaint by patients presenting for hearing loss treatment and this is only expected to grow as the population ages and noise exposure in our society continues to increase,” said Barbara Shinn-Cunningham, Ph.D., Director, Carnegie Mellon Neuroscience Institute and Cowan Professor of Auditory Neuroscience, Biomedical Engineering, Psychology, and Electrical & Computer Engineering at Carnegie Mellon University. “Extensive research conducted over the last decade suggests that damage to cochlear

synapses plays a role in this speech-in-noise hearing difficulty. Treatment with a neurotrophic factor such as BDNF offers potential for repair. I am encouraged by these initial results for OTO-413 across multiple speech-in-noise hearing tests and look forward to its continued development as an option for patients to regain functional hearing."

"We are excited to announce these positive top-line clinical results for OTO-413 that support its continued development for patients with hearing loss," said David A. Weber, Ph.D., president and CEO of Otonomy. "It is also a great way to build on the successful clinical trial results we announced this summer for OTO-313 in tinnitus, and further affirms our leading position in the emerging neurotology field. We continue to look forward to our third clinical catalyst with results from the Phase 3 trial of OTIVIDEX® in Ménière's disease still expected in the first quarter of 2021."

Webcast and Conference Call

Otonomy management will host a webcast and conference call regarding these clinical results at 8 a.m. ET today. The live call may be accessed by dialing (877) 305-6769 for domestic callers and (678) 562-4239 for international callers with conference ID code number: 9882298. A live webcast of the call will be available online in the investor relations section of Otonomy's website at www.otonomy.com and will be archived there for 30 days.

About Speech-in-Noise Hearing Difficulty

Recent scientific advances have shown that the loss of synaptic connections between inner ear hair cells and auditory nerve fibers contributes to hearing impairment. This cochlear synaptopathy is proposed as an underlying pathology in age-related and noise-induced hearing loss and is believed to contribute to the common difficulty of hearing speech in the presence of background noise. Overall, there are more than 50 million people in the U.S. with acquired hearing loss including a significant proportion experiencing speech-in-noise hearing difficulty, which can lead to social isolation, depression and early cognitive decline.

About the Phase 1/2 Trial

The Phase 1/2 trial was primarily intended to evaluate the safety of ascending doses of OTO-413 administered by a single intratympanic injection and secondarily to assess a clinical signal for OTO-413 across multiple speech-in-noise (SIN) hearing tests and other exploratory efficacy endpoints. The first three dose cohorts (0.01 mg, 0.03 mg, and 0.10 mg) each enrolled 8 subjects with a fourth dose cohort (0.30 mg) expanded to enroll 15 subjects. All cohorts were randomized 3:1 for OTO-413 or placebo. Subjects were evaluated at screening and baseline (pre-dose) and then again at Day 15, Day 29, Day 57 and Day 85 following treatment. The SIN tests included the Digits-in-Noise (DIN) test, Words-in-Noise (WIN) test, and American English Matrix test that uses sentences in background noise. Each of these SIN tests has been clinically-validated with a threshold level of improvement considered clinically meaningful. All 29 subjects treated with OTO-413 and 10 placebo subjects were included in the safety assessment. The top-line assessment of therapeutic activity was conducted in 9 evaluable OTO-413 subjects from the high dose cohort compared to 8 placebo subjects pooled from the last three dose cohorts.

About OTO-413

OTO-413 is a proprietary, sustained-exposure formulation of brain-derived neurotrophic factor (BDNF), which is a naturally occurring protein involved in neuron growth and repair. Nonclinical studies have demonstrated that local administration of BDNF repairs the connections between inner hair cells and auditory nerve fibers in the cochlea that are damaged due to noise trauma or exposure to ototoxic chemicals. Furthermore, Otonomy has demonstrated in preclinical studies that repair of synaptic connections is associated with a restoration of hearing function. The initial indication for OTO-413 is speech-in-noise hearing difficulty, a type of hearing loss believed to be caused by cochlear synaptopathy.

About Otonomy

Otonomy is a biopharmaceutical company dedicated to the development of innovative therapeutics for neurotology. The company pioneered the application of drug delivery technology to the ear in order to develop products that achieve sustained drug exposure from a single local administration. This approach is covered by a broad patent estate and is being utilized to develop a pipeline of products addressing important unmet medical needs including Ménière's disease, hearing loss, and tinnitus. For additional information please visit www.otonomy.com.

Cautionary Note Regarding Forward Looking Statements

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. Forward-looking statements generally relate to future events or the future financial or operating performance of Otonomy. Forward-looking statements in this press release include, but are not limited to, expectations regarding the potential benefits, patient population, development activity and advancement of Otonomy's clinical programs; statements relating to the timing of results of ongoing clinical trials; statements relating to potential treatment for patients suffering from hearing loss; statements by Barbara Shinn-Cunningham, Ph.D.; and statements by Otonomy's president and CEO. Otonomy's expectations regarding these matters may not materialize, and actual results in future periods are subject to risks and uncertainties. Actual results may differ materially from those indicated by these forward-looking statements as a result of these risks and uncertainties, including but not limited to: delays and disruption resulting from the COVID-19 pandemic and governmental responses to the pandemic, including current and future impacts to Otonomy's operations, the manufacturing of its product candidates, the progression of its current clinical trials, enrollment in its current and future clinical trials and patient conduct and compliance; Otonomy's ability to obtain additional financing; Otonomy's dependence on the regulatory success and advancement of its product candidates; the uncertainties inherent in the clinical drug development process, including, without limitation, Otonomy's ability to adequately demonstrate the safety and efficacy of its product candidates, and the nonclinical and clinical results for its product candidates, which may not support further development; the integrity of patient-reported outcomes in its current and future clinical trials; side effects or adverse events associated with Otonomy's product candidates; competition in the biopharmaceutical industry; Otonomy's dependence on third parties to conduct nonclinical studies and clinical trials; Otonomy's ability to protect its intellectual property in the United States and throughout the world; expectations regarding potential therapy benefits, market size, opportunity and growth; Otonomy's ability to manage operating expenses; implementation of Otonomy's business model and strategic plans for its business, products and technology; general economic and market conditions; and other risks. Information regarding the foregoing and additional risks may be found in the section entitled "Risk Factors" in Otonomy's Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission (the "SEC") on November 4, 2020, and Otonomy's future reports to be filed with the SEC. The forward-looking statements in this press release are based on information available to Otonomy as of the date hereof. Otonomy disclaims any obligation to update any forward-looking statements, except as required by law.

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