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AnGes' Phase 1b Trial Demonstrates Safety and Preliminary, Sustained Efficacy 12 Months After a Single Injection of NF-kappa B Oligo DNA Decoy in Subjects with Chronic Discogenic Low Back Pain

AnGes, Inc., a biopharmaceutical company focused on developing innovative gene-based medicines for serious diseases, announced today the top line clinical results on AMG0103, an investigational oligonucleotide drug for the treatment of chronic discogenic low back pain (DLBP). The data from all 25 men and women enrolled in the prospective, multi-center, double-blind, randomized and controlled study, ages 32 to 70 years (mean age: 53.5 yrs), indicate that the intradiscal injection of AMG0103 (NF-kappa B decoy oligo DNA) was well-tolerated, and no patients experienced serious adverse events (SAEs) throughout the 12-month course of study. In addition to the validation of drug safety in this first-in-human indication, the exploratory, prospectively-defined secondary efficacy endpoints also demonstrated clinically meaningful and statistically significant results with regard to back pain and patient satisfaction for 1 year.

Chronic discogenic low back pain is a ubiquitous problem for people worldwide and causes a high economic burden to societies, primarily due to lost productivity and wages. Low back pain is also the leading cause of living disability, exceeding major disorders such as depression, diabetes, vascular and respiratory disease. As a result of these demographics, and the debilitating nature of chronic DLBP, AMG0103 has a large market potential in this clinical indication.

"Based on the excellent safety profile, and long-term efficacy data from our Phase 1b study, we believe we may have a potential breakthrough therapy for select patients suffering from discogenic back pain," said Steven Garfin, MD, Principal Investigator of the study and Interim Dean of the UC San Diego School of Medicine where he has also served as Chairman of the Department of Orthopaedic Surgery since 1997. "Not only was the extent and 12-month duration of significant pain reduction impressive, but this is the first study to demonstrate restoration of intervertebral disc height. My colleagues and I look forward to further evaluation in subsequent trials. If successful, AMG0103 has the potential to be the first minimally invasive oligonucleotide decoy used in the treatment of this debilitating spinal condition."

Safety Results

The primary endpoint of the Phase 1b study was to assess the safety and tolerability of this investigational oligonucleotide decoy therapy in adults with DLBP through 12 months following treatment. This clinical trial was designed to evaluate increasing doses of AMG0103 (0.3, 3.0 and 10.0 mg) that, in an outpatient setting, were injected directly into the intervertebral disc. Based on the data through 12 months (Parts 1 & 2 of the study), there was no evidence of clinically relevant renal, hepatic or hematologic dysfunction. In addition, clinical examination of all patients through the 12-month endpoint (Part 2) confirmed the absence of neurologic, sensory or motor function decline in the placebo and all treatment groups.

Recently, AnGes completed their analysis of the 12-month safety data (Part 2) of this FDA-registered study, and interim results regarding the 12-month efficacy data will be discussed below. Among the 19 subjects receiving AMG0103, only a single, transient drug-related adverse event (AE) was observed in the immediate post-injection period, and this was a self-limiting instance of mild nausea in a subject in the low dose cohort. No subjects withdrew from the study as a result of AEs or SAEs related to the intervention or the drug itself. Based on observations over the course of the study, the

Medical Monitor and independent Data Safety Monitoring Board made no modifications to the protocol, and supported dose escalation across all three cohorts.

Results from Exploratory Efficacy Endpoints

Prospectively-defined secondary endpoints of the study included measurement of back pain, leg pain, and several validated instruments used to assess patient reported outcome measures such as the Patient Global Impression of Change (PGI-C), the Roland-Morris Disability Questionnaire (RMDQ) and the Oswestry Disability Index. Administration of AMG0103 resulted in a dose-dependent and sustained reduction in back pain, measured on a 100 mm VAS scale, throughout the 6-month, Part 1 study period. During Part 2, from 6 to 12 months, the 0.3 and 3.0 mg AMG0103 groups maintained improvement over baseline, and the 10 mg cohort demonstrated further pain reduction at the 9- and 12-month follow-up visits. While all doses showed clinical improvement compared to the placebo control, the subject group receiving a single 10 mg dose resulted in a reduction of back pain by almost 50% just 14 days after treatment. Back pain in this group continued to decline, reaching an 84% median reduction from baseline by 6 months, which was significantly better ($p=0.033$) than the placebo control group that showed just a 14% improvement. The VAS pain scores in this group continued to decline through 12 months, reaching a median reduction of 97.5% compared to baseline, which was also significantly better ($p=0.045$) than the control group. Given the relatively small sample size of each per protocol cohort ($n=6$) in this Phase 1b study, it is especially encouraging to see the preliminary signal of efficacy along with statistical significance in the 10 mg group.

A preliminary evaluation of potential changes in intervertebral disc height across all groups from baseline through the 6- and 12-month endpoints based on the available data was also performed. The placebo cohort's mean disc height declined 0.25 mm between the baseline and the 6-month review, correlating well with the published literature of preclinical models assessing potential therapies for DLBP. By contrast, the mean disc height of the 10 mg AMG0103 cohort increased 0.47 mm over the same period. This change was statistically significant ($p=0.021$), mirroring the preclinical results observed in peer-reviewed animal studies of AMG0103 presented to the US FDA as part of the regulatory process associated with execution of this clinical study. Analysis of the complete 6 and 12 month radiographs to assess disc height changes has yet to be completed. While the clinical improvements in back pain and PGI-C of the 10 mg cohort parallels this change in disc height, it is premature to draw a direct conclusion that this structural change is responsible for the statistically significant improvement in patient reported outcomes.

For patient reported outcomes, the PGI-C score (measured from 1 to 7 on an ordinal scale) revealed a dose-dependent improvement from baseline at 6 months, and the 10 mg cohort was superior to placebo control at all time points through 12 months. In the 10 mg AMG0103 cohort, the improvement was almost 3 full points better than that observed with the control at 6 months, and was statistically significant at 6 ($p=0.001$) and 12 months ($p=0.042$). The PGI-C instrument quantifies how patients regard their improvement from baseline. As such, and using the 7- point scale, the 5-point improvement of the 10 mg cohort at 6 and 12 months is clinically significant. In addition to this outcome, all three treatment arms showed a 20 to 50% mean improvement in RDMQ score at 6 months while the control arm declined more than 15% from baseline. At 12 months, the 10 mg AMG0103 cohort still showed a 38% mean improvement over baseline, while the control group declined by 45%.

Patients enrolled in this study were not allowed to self-medicate with opioids at any time, but were allowed to use oral non-steroidal anti-inflammatory drugs (NSAIDs) or acetaminophen for breakthrough pain. Subjects were required to cease these "Rescue Medications" prior to follow-up visits, and their drug use diary was examined at each visit to record the frequency of use. Patients in the placebo control group used Rescue Medications on an average of 16 days throughout the 12-month study, with a maximal use of 98 days by one subject in that cohort. By contrast, not a single subject in the 10 mg AMG0103 cohort ever required or took a single Rescue Medication during the

course of the study. The avoidance of additional pharmaceutical intervention, whether NSAIDs or other drugs, further highlights the clinical benefit demonstrated in this Phase 1b clinical trial.

“Taken together, we believe these data support the assertion that a single 10mg intradiscal dose of AMG0103 can lead to significant, safe and long-lasting improvements in back pain, patient satisfaction, intervertebral disc structure, as well as a reduction in the use of oral pain medication” said Dr. Ei Yamada, Chief Executive Officer of AnGes, Inc. “We want to give our heartfelt thanks to all the patients, researchers, investigators and their staff for their passion, expertise and engagement in helping to advance this clinical research. We plan to advance our clinical study program to confirm these preliminary results in order to obtain marketing approval from the FDA and possibly other regulatory agencies around the world.”

About AMG0103

AMG0103 is an investigational, synthetic NF-kB oligonucleotide decoy that binds the NF-kB transcription factor to suppress release of inflammatory cytokines (physiologically active substances that are secreted by cells) and therefore has the potential to become an effective therapeutic agent for the treatment of various disorders caused by excessive inflammatory reactions and immune responses. Currently, the only pharmaceutical therapy approved by the US FDA for chronic DLBP is symptomatic treatment by anti-inflammatory analgesics. AMG0103 differs from existing analgesics because it exerts its effect by inhibiting the presumptive causative agent. The results of basic scientific research suggest that local injection of AMG0103 is also effective in treating intervertebral disc degeneration, helping restore disc height, and suppressing the progression of the disease, which cannot be treated with existing therapeutic agents.
AnGes will continue its efforts to develop this groundbreaking therapeutic agent for the treatment of chronic DLBP.

About AnGes

AnGes, Inc., a biopharmaceutical company focuses on the development of gene-based medicines. In September 2019, AnGes commenced the commercialization in Japan of Collategene® (Hepatocyte Growth Factor, HGF, plasmid gene therapy) for the treatment of Chronic arterial occlusive disease with lower limb ulcers. Collategene® is the world’s first marketed drug using Plasmid DNA. AnGes is currently focusing on the development of DNA vaccines for COVID-19 and Hypertension, Tie2 tyrosine kinase receptor agonist for COVID-19 treatment, and NF-κB decoy oligonucleotide and Chimera decoy oligonucleotide as next generation product for Chronic Discogenic Lumbar Back Pain. Furthermore, AnGes acquired EmendoBio to expand its capabilities in Genome Editing Technologies in December 2020. For more information, visit https://www.anges.co.jp/en/

The company is located in Tokyo and Osaka, Japan and listed on Mothers of Tokyo Stock Exchange, a market for emerging companies.

Forward-Looking Statement

This news release contains forward-looking statements. Any forward-looking statements are based on the current expectations of the company’s management and are subject to significant risks and uncertainties.

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