ArmaGen's AGT-181 52-Week Phase 1/2 Proof-of-Concept Study Results Published in *Orphanet Journal of Rare Diseases*

Novel Fusion Protein Demonstrates Neurocognitive Benefit in Children with Severe Mucopolysaccharidosis Type I (MPS I, or Hurler Syndrome), with Favorable Safety Profile

Data Validate ArmaGen's Platform Technology for Blood-Brain Barrier Transport of Biologics

Calabasas, Calif., July 10, 2018 – ArmaGen, Inc., a privately held biotechnology company focused on developing groundbreaking therapies to treat severe neurological disorders, today released the full results from a 52-week Phase 1/2 proof-of-concept study of AGT-181 (valanafusp alpha) in patients with severe MPS I. AGT-181 is the company's investigational therapy for the treatment of mucopolysaccharidosis type I (MPS I, also known as Hurler, Hurler-Scheie and Scheie syndromes). The data, appearing in the current issue of the *Orphanet Journal of Rare Diseases (OJRD)*, suggest that AGT-181 stabilizes neurocognitive development in children with severe MPS I, and has a favorable safety and tolerability profile. Several patients previously treated with laronidase experienced an unexpected and positive somatic benefit. Finally, the results also validate the ability of ArmaGen's proprietary drug delivery technology to transport biopharmaceuticals across the blood-brain barrier (BBB) and provide therapeutic benefit to patients with severe MPS I.

"The *OJRD* publication provides important clinical validation of ArmaGen's 'Trojan Horse' platform, which enables efficient and targeted delivery of enzyme replacement therapy across the blood-brain barrier and into the central nervous systems and peripheral organs of children with MPS I, thereby stabilizing neurocognitive function," said William Pardridge, M.D., Founder and Chief Scientific Officer of ArmaGen. "These results solidify ArmaGen's place as the leader in BBB transport and delivery and we look forward to leveraging our platform to advance additional programs into clinical development."

In their paper, entitled, "Neurocognitive and somatic stabilization in pediatric patients with severe Mucopolysaccharidosis Type I after 52 weeks of intravenous brain-penetrating insulin receptor antibody-iduronidase fusion protein (valanafusp alpha): An open label phase 1-2 trial," a team of investigators led by Roberto Giugliani, M.D, Ph.D., reported that one-year treatment with AGT-181:

- Stabilizes several measures of neurocognitive function including the neurocognitive development quotient (DQ) – a numerical indicator of a child's growth to maturity across a range of cognitive competencies – and the cortical grey matter volume of brain in children
- Stabilizes or improves somatic (i.e., those pertaining to body parts and systems other than the brain) manifestations of MPS I, based on urinary glycosaminoglycan levels, hepatic and spleen volumes, and shoulder range of motion
- Has a favorable long-term safety and tolerability profile. The most frequent drug-related adverse events in the Phase 1/2 trial were infusion reactions (1.7%) and transient hypoglycemia (2.1% at 1 mg/kg and 3 mg/kg)

In the Phase 1 portion of the trial, six adults with attenuated MPS I received AGT-181 at doses of 0.3, 1, and 3 milligrams per kilogram of body weight (mg/kg) via intravenous (IV) infusion. In the Phase 2 portion, 11 children (aged 2-15 years) underwent treatment with AGT-181 at doses of 1, 3, or 6 mg/kg for 52 weeks. Preliminary results were previously presented at the 14th Annual WORLD*Symposium* earlier this year.

"We were very excited to see the stabilization in the cognitive domain of the development quotient, which fell by a mean of only 1.2 points over 52 weeks of AGT-181 therapy. That contrasts sharply with the expected 10-20-point drop over one year that is typically seen in patients with severe MPS I who have not undergone successful hematopoietic stem cell transplantation," commented Dr. Giugliani, who is affiliated with Hospital de Clínicas in Porto Alegre, Brazil. "AGT-181 therefore appears to stabilize neurocognitive function to the same extent as stem cell transplantation, which must be performed before the age of 16

months to achieve this effect. That we were able to observe stabilization in children aged 2 years and older suggests that AGT-181 can be a viable option for this underserved patient population."

Dr. Giugliani and colleagues also reported stabilization of cortical grey matter volume at 52 weeks of AGT-181 therapy. Among the nine patients previously on laronidase enzyme replacement therapy (ERT) for 1-12 years, AGT-181 was associated with further improvements in somatic disease control, based on further reductions in liver and spleen volume, and increases in shoulder flexion and extension range of motion. The anti-drug antibody (ADA) profile with AGT-181 treatment was comparable to that observed with laronidase in prior studies.

AGT-181 was well tolerated. Out of more than 570 infusions, there were 10 infusion-related reactions (IRRs) – an incidence rate of 1.7%. Sixty percent of IRRs were observed in a single patient not previously treated with ERT; this patient developed tolerance to AGT-181 by the tenth week of therapy. Other drug-related adverse events (AEs) included transient hypoglycemia (6.4% incidence), which resolved within 10-20 minutes following a snack or glucose administration. Most hypoglycemic events (67%) occurred in patients taking high-dose (6 mg/kg) AGT-181 therapy. Among patients receiving an infusion dose of 1-3 mg/kg, the incidence of hypoglycemia was 2.1%. The investigators observed no serious AEs that were likely to be drug-related.

About Mucopolysaccharidosis I (MPS I)
MPS I is a rare, hereditary, lysosomal storage disease that arises from a deficiency or absence of the enzyme iduronidase (IDUA), which is needed to break down complex sugars produced by the body. MPS I affects approximately 3,000-4,000 patients worldwide. The most severe form of MPS I, Hurler syndrome, affects several organs including the brain, resulting in somatic and neurological manifestations that can include developmental delay, progressive mental decline, loss of physical function, impaired language development, airway obstruction, corneal and retinal damage, carpal tunnel syndrome, and restricted joint movement. Attenuated or less severe forms of MPS I include Hurler-Scheie and Scheie syndromes. Patients with Hurler-Scheie syndrome may suffer from mild cognitive impairment or problems with attention. Patients with Scheie syndrome generally have a later onset, milder symptoms, and a slower disease progression, usually without CNS involvement, although they can develop significant morbidity.

About AGT-181
AGT‑181 is a novel, investigational enzyme replacement therapy for the treatment of both somatic and cognitive symptoms in patients with MPS I. ArmaGen developed AGT-181 by re-engineering the enzyme iduronidase (IDUA) as fusion protein with an immunoglobulin G (IgG) antibody targeting the insulin receptor. Utilizing ArmaGen's proprietary "Trojan Horse" technology, AGT-181 takes advantage of the body's natural system for transporting proteins and other large molecules non-invasively across the blood-brain barrier (BBB), in this case by binding the same receptor that transports insulin across the BBB into the brain.

In November 2017, the U.S. Food and Drug Administration (FDA) granted Fast Track designation to AGT-181. A Fast Track designation is aimed at accelerating the development and regulatory review of drugs meeting urgent needs. To receive the designation, a therapy candidate must demonstrate an advantage over currently available treatments such as superior efficacy, ability to meet an unmet medical need, or fewer side effects.

About ArmaGen
ArmaGen, Inc., is a privately held biotechnology company focused on developing groundbreaking therapies for severe neurological disorders. The company is developing a robust pipeline of innovative therapies for the treatment of lysosomal storage disorders including neurological symptoms such as Hurler syndrome (MPS I), Hunter syndrome (MPS II), metachromatic leukodystrophy, Sanfilippo A and B syndromes, as well as other diseases with severe CNS manifestations. ArmaGen's pipeline is based on decades of scientific leadership in engineering therapies to cross the blood-brain barrier and a dominant intellectual property portfolio. The company is advancing its pipeline through licensing and collaboration agreements, in-house development programs, and other partnering opportunities. For more information, visit www.armagen.com.

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