



## ArmaGen's AGT-181 Demonstrates Neurocognitive Benefit in Children with Severe MPS I

*Full 52-Week Results from Phase 2 Proof-of-Concept Trial Presented at 2018 WORLDSymposium*

*Data Confirm Previous Findings of the Ability to Cross the Blood-Brain Barrier with ArmaGen's Proprietary Drug Delivery Technology*

**Calabasas, Calif., February 8, 2018** – ArmaGen, Inc., a privately held biotechnology company focused on developing groundbreaking therapies to treat severe neurological disorders, today reported full 52-week results from a Phase 2 proof-of-concept study with AGT-181, the company's investigational therapy for the treatment of mucopolysaccharidosis type I, or MPS I (also known as Hurler, Hurler-Scheie and Scheie syndromes). Data presented today at the 14<sup>th</sup> Annual WORLDSymposium in San Diego, California, suggest that AGT-181 stabilized the neurocognitive development quotient (DQ) in patients with severe MPS I. The data validate previous findings that demonstrated 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.

In an oral presentation entitled, "Safety and clinical efficacy of AGT-181, a brain penetrating human insulin receptor antibody-iduronidase fusion protein, in a 52-week study with pediatric patients with mucopolysaccharidosis type I," Roberto Giugliani, M.D., Ph.D., of Hospital de Clínicas in Porto Alegre, Brazil, reported the following:

- Stabilization of several measures of neurocognitive function as measured by DQ -- a numerical indicator of a child's growth to maturity across a range of cognitive competencies -- in children treated with AGT-181 for one year
- On a somatic level, AGT-181 stabilized urinary glycosaminoglycans, reduced liver and spleen volume including in patients previously exposed to laronidase, and further improved shoulder range of motion
- AGT-181 displayed a favorable long-term safety and tolerability profile. Most frequent drug-related adverse events were infusion reactions (1.7%) and transient hypoglycemia (2.8% at 1 mg/kg and 3 mg/kg).

"The full results from this Phase 2 study validate our preliminary findings that AGT-181 crosses the blood-brain barrier and benefits neurocognitive function in children with severe MPS I," said Dr. Giugliani. "Whereas the existing enzyme replacement therapy improves many of the somatic manifestations of MPS I, its inability to cross the blood-brain barrier prevents it from addressing the severe and progressive neurological symptoms of the most severe form of the disorder. Now that we have demonstrated proof of concept, a controlled phase 3 clinical trial is warranted to examine long term impact in cognition in MPS I patients with CNS involvement."

At the 13<sup>th</sup> Annual WORLDSymposium in 2017, Dr. Giugliani presented preliminary evidence of cognitive improvement in age-equivalent function in the first five children with MPS I who were enrolled in the Phase 2 study, after six months of treatment with AGT-181. This year's presentation included the full set of 52-week data from all 11 children (age 2 years or older) enrolled in the trial. Nine of eleven patients had previously been treated with enzyme replacement therapy and one had received a stem cell transplant which had failed engraftment. The children received weekly intravenous infusions of AGT-181 at doses of 1.0, 3.0 or 6.0 mg/kg. The investigators conducted developmental age-appropriate neurocognitive testing at 13, 26 and 52 weeks of treatment, utilizing the following validated neurocognitive assessments tests: the Bayley Scales of Infant Development Third Edition (BSID-III) or the Kaufman Assessment Battery for Children (KABC-II), and the Vineland Adaptive Behavior Scales Second Edition (VABS-II). Together, these tests represent a summation of scores reflecting cognitive, language and motor skills.

Dr. Giugliani reported stabilization of the cognitive DQ with no net decline after 52 weeks of AGT-181, as would normally be expected for the severe MPS I patients that have not undergone successful hematopoietic stem cell transplantation. He also presented stabilization of cortical grey matter volume at

52 weeks of AGT-181 therapy. Among the nine patients previously on laronidase 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. Additionally, the anti-drug antibody (ADA) profile with AGT-181 treatment was comparable to that observed with laronidase, Dr. Giugliani reported.

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 on ERT; this patient developed tolerance to AGT-181 by the tenth week of therapy. Other drug-related adverse events (AEs) included transient hypoglycemia (5.9% incidence) that resolved within 10-20 minutes following a snack or glucose administration. Most hypoglycemic events (62%) 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 2.8%. The investigators observed no serious AEs that were likely to be drug-related.

“By confirming our initial findings of neurocognitive stabilization/improvement in children with MPS I, the full results from the Phase 2 proof-of-concept trial – coupled with our recent receipt of a Fast Track designation from the FDA – sustain the momentum of finding a new treatment option for patients with MPS I,” said Mathias Schmidt, Ph.D., Chief Executive Officer of ArmaGen. “The latest results add to the growing body of evidence that our proprietary ‘Trojan Horse’ technology can deliver the missing enzyme into the CNS of patients and benefit neurocognitive function. We are most grateful to the patients and families who participated in the Phase 2 study.”

### **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](http://www.armagen.com).

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