



Attune Pharmaceuticals Announces Pre-Clinical Data for ATN-249, An Oral Plasma Kallikrein Inhibitor for the Treatment of HAE at AAAAI

NEW YORK, NY. -- March 6, 2017 — Attune Pharmaceuticals, a biotechnology company focused on the discovery and development of novel oral small molecule therapeutics for treatment of rare diseases, announced today the first preclinical data results for ATN-249, a novel orally administered plasma kallikrein inhibitor for the treatment of Hereditary Angioedema (HAE). The data was presented today in a late-breaking poster presentation at the 2017 American Academy of Allergy, Asthma & Immunology Annual Meeting (AAAAI 2017) and highlighted a profile which suggests high potency with a wide therapeutic window and the potential for once daily dosing of ATN-249.

Studies demonstrated ATN-249 was highly selective and potent at plasma kallikrein inhibition in both biochemical inhibition and contact activation assays. “We are pleased with the performance of ATN-249, in particular the relative activity against C1-INH, the standard of care in the relevant pre-clinical assays for kallikrein inhibition,” said Dr. Andrew McDonald, CEO of Attune Pharmaceuticals, “The data we have seen to date indicates that this lead drug candidate may be a potent, safe, orally-administered plasma kallikrein inhibitor for treatment of HAE and we intend to start Phase I in 2017.”

The poster outlined the results of several well-established preclinical assays. The studies included evaluation of selectivity by biochemical inhibition on plasma kallikrein relative to other serine proteases, potency by biochemical inhibition and contact activation assays in human plasma, and pharmacokinetic exposure in monkeys after a single oral administration of ATN-249.

Study Results:

- **SELECTIVITY:** ATN-249 was >2000-fold more selective at inhibiting plasma kallikrein versus other closely related serine proteases, including tissue kallikrein 5, plasmin, Factor Xa, Factor VIIa, thrombin, and tissue plasminogen activator (tPA)
- **POTENCY:** ATN-249 demonstrated ~10-fold greater plasma kallikrein inhibition relative to C1-INH in both biochemical inhibition and contact activation assays — an ex-vivo assay that closely represents clinical pharmacology
 - In biochemical inhibition, ATN-249 had an IC₅₀ of 2.7nM versus 25.4nM for C1-INH
 - In contact activation assays, ATN-249 had an EC₅₀ of 8.2nM versus 92.4nM for C1-INH
- **PHARMACOKINETICS:** A single oral dose of ATN-249 at 15mg/kg provided 24-hour exposure 30-fold greater than EC₅₀



- **SAFETY:** No adverse events were observed at the highest dose (300mg/kg) when evaluated in 14-day non-GLP rat and monkey toxicology studies; safety evaluation in 28-day GLP studies are ongoing

Based on the positive performance and excellent pre-clinical safety profile, Phase 1 clinical studies of ATN-249 are expected to start in the middle of this year to evaluate ATN-249's safety, tolerability and pharmacokinetic profile in healthy volunteers.

About Hereditary Angioedema

Hereditary angioedema (HAE) is a rare, potentially life-threatening disease characterized by acute skin and mucosal edema. It is caused by an autosomal dominant mutation of the SERPING1 or F12 genes, resulting in diminished C1 inhibitor levels and/or function. Dysregulation of the contact-kallikrein pathway mediated by dysfunctional C1 inhibitor causes upregulation of bradykinin production, leading to increased vascular permeability, recurrent abdominal pain, and mucosal swelling, which can be fatal with laryngeal involvement. Current treatments are limited by route of administration and adverse events, since all HAE drugs are administered intravenously or subcutaneously, and may be associated with drug-specific adverse effects.

About Attune Pharmaceuticals

Attune Pharmaceuticals is a pre-clinical stage biotechnology focused on the discovery and development of novel oral once-daily small molecule therapeutics for treatment of rare diseases. Attune Pharmaceuticals is currently developing 2 programs in rare diseases: Hereditary Angioedema (HAE) and complement-mediated diseases. Attune Pharmaceuticals has identified ATN-249 as a lead candidate to treat HAE and will begin clinical testing in 2017.

About ATN-249's Clinical Development Program

ATN-249 was designed as a novel, potent, selective, and orally-administered plasma kallikrein inhibitor for the treatment of Hereditary Angioedema (HAE) by blocking kallikrein-mediated production of bradykinin. Preclinical studies in both biochemical and contact activation assays have demonstrated that ATN-249 is highly selective and potent at plasma kallikrein inhibition. ATN-249 has been evaluated in several pharmacokinetic and toxicological studies in multiple species. Given its observed wide therapeutic window and once-daily dosing potential, these preclinical results suggest that ATN-249 may be a potent, safe, orally-administered plasma kallikrein inhibitor for the treatment of HAE.

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