Pandion Therapeutics Announces Positive Top-Line Phase 1a Clinical Data Showing PT101 was Well-Tolerated and Selectively Expanded Regulatory T cells

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-Phase 1a trial achieved primary objective of safety and tolerability
-PT101 induced potent and selective expansion of regulatory T cells exceeding levels associated with clinical benefit in third-party clinical trials across multiple autoimmune diseases
-PT101 maintained selectivity for regulatory T cells at all doses tested
-Phase 1a/2b clinical trial in ulcerative colitis expected to start mid-2021 and Phase 2 clinical trial in systemic lupus erythematosus expected to start second half 2021
-Phase 1a results to be presented in a conference call scheduled today at 8:30 a.m. ET

WATERTOWN, Mass., Jan. 04, 2021 (GLOBE NEWSWIRE) -- Pandion Therapeutics (Nasdaq: PAND) today announced positive top-line data from its Phase 1a single-dose, healthy volunteer clinical trial, demonstrating proof of mechanism of PT101, an engineered IL-2 mutein fused to a protein backbone, in development for ulcerative colitis (UC), systemic lupus erythematosus (SLE), and other autoimmune diseases.

In the Phase 1a clinical trial, PT101 was observed to be well-tolerated and there were no serious adverse events.

PT101 selectively expanded total regulatory T cells (Tregs), with a mean maximal increase up to of 3.6-fold over baseline. A subset of activated Tregs with high CD25 expression, known as CD25 bright Tregs, expanded, with a mean maximal increase of up to 72.5-fold over baseline. There was no evidence of expansion of natural killer T (NK) cells and pro-inflammatory conventional T (Tconv) at any dose studied. In third-party clinical trials using low-dose native IL-2, a two-fold increase in total Tregs was associated with clinical benefit across multiple autoimmune diseases.

“Native IL-2 has been the subject of several clinical trials across a range of autoimmune diseases due to its ability to activate a normal immune regulatory response and improve disease activity. However, its therapeutic use has been hampered by native IL-2’s undesired activation of the pro-inflammatory side of the immune system,” said Scott Snapper, M.D., Ph.D., Chief, Division of Gastroenterology, Hepatology and Nutrition; Director, Inflammatory Bowel Disease Center at Boston Children’s Hospital and Professor of Medicine at Harvard Medical School. “PT101’s high selectivity for and expansion of Tregs could allow for a fulsome exploration of the potential of this mechanism in autoimmune diseases, and I look forward to seeing its continued clinical development by Pandion.”

The Phase 1a randomized, blinded clinical trial enrolled 56 healthy volunteers across seven cohorts who each received a single subcutaneous fixed dose of PT101 ranging from 1 mg to 10 mg, or placebo. Subjects were followed for 28 days after dosing and evaluated for safety and tolerability as well as pharmacokinetic and pharmacodynamic measures. These measures were selected to assess the potency and selectivity of PT101 in order to establish proof of mechanism.

All adverse events observed in the trial were low grade (Grade 1 or 2) and self-limited. The most common adverse events were skin reactions of itching, redness or pain near or around the site of injection of PT101. In laboratory tests, some subjects showed transient elevations of eosinophils, a type of white blood cell, that were self-limited in nature and did not require medical treatment. The Company believes the eosinophil elevation may be related to the IL-2 mechanism of PT101.

Expansion of both total Tregs and the CD25 bright Treg subset was observed throughout the dose range, as depicted in the table below. Peak expansion of Tregs was observed between days 8 and 10. At doses of 3.5 mg and above, PT101 induced a two-fold or greater expansion of total Tregs in more than 80% of subjects. Tregs returned to baseline or near-baseline over the 28-day follow-up period, supporting the Company’s plan to utilize a dosing regimen of every four weeks in future clinical trials.

	Placebo (n=14)	1 mg (n=6)	3.5 mg (n=12)	5 mg (n=12)	7.5 mg (n=6)	10 mg (n=6)
Mean peak fold expansion of Total Tregs (SEM)	1.4 (±0.08)	1.8 (±0.31)	3.6 (±0.66)	3.5 (±0.37)	3.4 (±0.57)	3.2 (±0.24)
Mean peak fold expansion of CD25 bright Treg subset (SEM)	3.4 (±0.49)	8.6 (±3.33)	72.5 (±26.39)	54.1 (±8.89)	51.6 (±17.17)	37.4 (±6.93)

SEM= standard error of the mean

“These data show PT101 meaningfully expanded regulatory T cells while maintaining a high degree of selectivity,” commented John Sundy, M.D., Ph.D., Chief Medical Officer of Pandion Therapeutics. “We believe this combined potency and selectivity could provide meaningful clinical benefit for patients with many different autoimmune diseases. Therefore, following the completion of the regulatory process, we plan to initiate a Phase 1b/2a clinical trial in patients with UC in mid-2021 and a Phase 2 clinical trial in patients with SLE in the second half of 2021.”

Full data from the trial are expected to be presented at upcoming medical meetings.

Conference Call and Webcast Information
Pandion will hold a conference call and webcast to review the Phase 1a clinical data of PT101 today at 8:30 a.m. ET. To participate in the conference

call, please dial +1 833-693-0533 (US toll-free number) or +1 661-407-1572 (international participants) and use the passcode 6051816. Investors may also access a live audio webcast of the call and slides for the discussion via the Investors & News section of the Company's website, www.pandiontx.com. A replay of the webcast will be available on the Company's website shortly after the presentation ends.

About Regulatory T Cells (Tregs)
Tregs act as a control node within the immune system and can inhibit the activity of several different pro-inflammatory immune cell types. Tregs are critical for self-tolerance, or the ability of the immune system to recognize a hosts' cells and not produce an immune attack against them. Defects in Tregs result in multi-organ inflammation and their dysfunction is associated with many autoimmune diseases. Multiple third-party clinical trials suggest that expansion of Tregs by low-dose IL-2 can benefit patients with autoimmune diseases.

CD25 bright Tregs are a subset of Tregs with high expression of CD25 (also known as the IL-2 receptor alpha subunit). It has been reported that CD25 bright Tregs may be a more active subset of Tregs with enhanced immune regulatory function.

About PT101
PT101 is an engineered IL-2 mutein fused to a protein backbone designed to selectively activate and expand regulatory T cells for the treatment of autoimmune diseases. In autoimmune diseases, the immune system inappropriately attacks a host's cells, and targeting regulatory T cells could allow the immune system to regain control and return to homeostasis. PT101 has completed a Phase 1a clinical trial, which met its primary endpoint of safety and tolerability. In the trial, PT101 demonstrated proof of mechanism by selectively expanding Tregs in healthy volunteers.

About Pandion Therapeutics
Pandion Therapeutics is developing novel therapeutics designed to address the unmet needs of patients living with autoimmune diseases. Pandion's TALON (Therapeutic Autoimmune reguLatOry proteiN) drug design and discovery platform enables the company to create a pipeline of product candidates using immunomodulatory effector modules, with the ability to also combine an effector module with a tissue-targeted tether module in a bifunctional format. Pandion's lead product candidate PT101, a combination of an interleukin-2 mutein effector module with a protein backbone, is designed to selectively expand regulatory T cells systemically, without activating proinflammatory cells, such as conventional T cells and natural killer cells. Pandion is continuing to develop and expand its library of effector and tether modules as part of its earlier-stage research and discovery pipeline. For more information, please visit www.pandiontx.com and engage with us on Twitter @PandionTX or on LinkedIn.

Forward-Looking Statements
This press release contains "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995 that involve substantial risks and uncertainties. All statements, other than statements of historical facts, contained in this press release, including statements regarding PT101 as a potential treatment for patients with autoimmune diseases, the timing of future clinical trials of PT101, the Company's strategy and clinical development plans, timelines and prospects, are forward-looking statements. The words "anticipate," "believe," "continue," "could," "estimate," "expect," "intend," "may," "plan," "potential," "predict," "project," "should," "target," "will," "would" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Any forward-looking statements are based on management's current expectations of future events and are subject to a number of risks and uncertainties that could cause actual results to differ materially and adversely from those set forth in, or implied by, such forward-looking statements. These risks and uncertainties include, but are not limited to, risks associated with Pandion's ability to obtain and maintain necessary approvals from the FDA and other regulatory authorities; initiate preclinical studies and clinical trials of PT101 and its other product candidates; advance PT101 and its other product candidates in preclinical research and clinical trials; replicate in clinical trials positive results found in preclinical studies; advance the development of its product candidates under the timelines it anticipates in current and future clinical trials; obtain, maintain or protect intellectual property rights related to its product candidates; manage expenses; and raise the substantial additional capital needed to achieve its business objectives. For a discussion of other risks and uncertainties, and other important factors, any of which could cause the Company's actual results to differ from those contained in the forward-looking statements, see the "Risk Factors" section, as well as discussions of potential risks, uncertainties and other important factors, in the Company's most recent filings with the Securities and Exchange Commission. In addition, the forward-looking statements included in this press release represent the Company's views as of the date hereof and should not be relied upon as representing the Company's views as of any date subsequent to the date hereof. The Company anticipates that subsequent events and developments will cause the Company's views to change. However, while the Company may elect to update these forward-looking statements at some point in the future, the Company specifically disclaims any obligation to do so.

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