AnaptysBio Announces Positive Rosnilimab Healthy Volunteer Phase 1 Top-Line Data

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- Rosnilimab, AnaptysBio's wholly-owned anti-PD-1 agonist antibody, demonstrated favorable safety and tolerability in single and multiple ascending dose healthy volunteer cohorts
- Robust pharmacokinetic profile, in conjunction with rapid and sustained PD-1 receptor occupancy
- Pharmacodynamic activity resulted in dose-dependent reduction of PD-1+ T cells and antigen-specific immune response, which we believe supports rosnilimab's potential to treat T-cell driven human inflammatory diseases
- Data support monthly subcutaneous rosnilimab dosing in upcoming AZURE Phase 2 placebo-controlled clinical trial in moderate-to-severe alopecia areata patients

SAN DIEGO, Nov. 15, 2021 (GLOBE NEWSWIRE) -- AnaptysBio, Inc. (Nasdaq: ANAB), a clinical-stage biotechnology company developing first-in-class antibody product candidates focused on emerging immune control mechanisms applicable to inflammation and immuno-oncology indications, today announced positive top-line data from a randomized placebo-controlled healthy volunteer single and multiple ascending dose Phase 1 trial of rosnilimab, its investigational wholly-owned anti-PD-1 agonist therapeutic antibody, previously known as ANB030. Top-line data demonstrated favorable safety, pharmacokinetics and pharmacodynamic results that support advancement of rosnilimab into subsequent patient trials.

"Agonizing the inhibitory function of PD-1 is an exciting new approach to T cell modulation," said Dr. W. Michael Gallatin, leading anti-inflammatory drug development expert and member of AnaptysBio's Research and Development Committee. "These data support rosnilimab's potential to specifically target the subset of T cells expressing PD-1 which are believed to be key drivers of human autoimmune and inflammatory diseases."

"We are pleased to report promising results for rosnilimab in this healthy volunteer Phase 1 trial," said Dr. Paul F. Lizzul, chief medical officer of AnaptysBio. "We believe rosnilimab's mechanism is broadly applicable to T cell driven inflammatory diseases and look forward to initiating our AZURE moderate-to-severe alopecia areata trial."

A total of 144 subjects were enrolled in the randomized, double-blind, placebo-controlled healthy volunteer Phase 1 trial, where single ascending dose (SAD) cohorts were administered single subcutaneous or intravenous doses of rosnilimab ranging between 0.02mg to 600mg or placebo, while multiple ascending dose (MAD) cohorts received four weekly subcutaneous doses of rosnilimab ranging between 60mg and 400mg or placebo. Dose escalation was conducted subsequent to data safety monitoring board review of safety and tolerability parameters following each single and multiple ascending dose level.

Rosnilimab was generally well-tolerated and no dose limiting toxicities were observed. The most frequent adverse event reported among SAD cohorts was increased circulating C-reactive protein levels of mild severity in nine (10%) rosnilimab-dosed subjects occurring sporadically in a dose-independent manner and a severe occurrence in one (3.3%) placebo-dosed subject. MAD cohorts reported headache as the most frequent adverse event with mild occurrences in three (12.5%) rosnilimab-dosed subjects and none in placebo subjects. Mild injection site reactions were observed in two subjects (11.1%) administered with multiple subcutaneous rosnilimab doses. Two serious adverse events were reported in single dose cohorts, including obstructive pancreatitis in a placebo-dosed subject and COVID-19 infection in a rosnilimab-dosed subject leading to discontinuation which was deemed unrelated to treatment. No serious adverse events were reported in subjects receiving multiple doses of rosnilimab or placebo.

Pharmacokinetic analyses demonstrated a favorable profile for rosnilimab with an estimated two-week half-life for subcutaneous and intravenous routes of administration and approximately 80% bioavailability. Low-titer anti-drug antibodies were detected at low single dose levels in 19 (21%) rosnilimab-dosed subjects, but none were detected in high single dose or multiple dose subjects. Full PD-1 receptor occupancy was observed rapidly during the first week following single subcutaneous rosnilimab doses at or above 60mg, and was maintained for at least 30 days at or above 200mg single subcutaneous doses. These data support monthly subcutaneous dosing of rosnilimab for future patient trials.

T Cell Population	Surface Markers	Average Change From Baseline
Total T (Tcon and Treg) cells	CD3+	<5% change
Conventional T (Tcon) cells	CD3+, CD25low	<5% change
PD-1 expressing Tcon cells	CD3+, CD25low, PD-1+	50% reduction
High PD-1 expressing Tcon cells	CD3+, CD25low, PD-1high	90% reduction

Total regulatory T (Treg) cells	CD3+, CD4+, CD25bright, CD127-	<5% change

Table 1. Approximate average change in T cell populations relative to baseline in SAD cohorts achieving full receptor occupancy between Day 5 and Day 29 following rosnilimab treatment.

Rosnilimab's pharmacodynamic activity resulted in rapid and sustained reduction in the quantity and functional activity of PD-1+ T cells, which are known to be pathogenic drivers of inflammatory diseases. Conventional T (Tcon) cells (CD3+, CD25 low) expressing PD-1, which represented approximately 25% of peripheral T cells at baseline, were reduced by 50%, including in both CD4+ and CD8+ subsets, in a dose-dependent manner and in correlation with receptor occupancy (Table 1). This effect was maximized on high-PD-1 expressing Tcon cells, which represented approximately 5% of peripheral T cells, with 90% reduction relative to baseline. Conversely, total T cells (CD3+), total Tcon cells (CD3+, CD25low) and total regulatory T (Treg) cells (CD3+, CD4+, CD25 bright, CD127-) were unchanged (<5% change from baseline), resulting in a favorable shift in the ratio of PD-1+ Tcon cells to total Treg cells post-treatment. No effect (<5% reduction from baseline) was observed on any of the aforementioned cell types in placebo-dosed subjects. In addition, an antigen-specific functional T cell recall response, measured as *ex vivo* interferon-gamma released in response to tetanus toxoid challenge, was inhibited in a receptor occupancy dependent manner and was consistent with the observed reduction of PD-1+ Tcon cells, to a maximum of approximately 90% relative to baseline within 30 days following single rosnilimab dose, while placebo administration had no effect. Based upon these data, we believe rosnilimab's *in vivo* mechanism has the potential to treat T-cell driven human inflammatory diseases.

About Rosnilimab
Rosnilimab is a wholly-owned PD-1 agonist antibody developed by AnaptysBio using its somatic hypermutation technology platform. Genetic studies have demonstrated that PD-1 pathway mutations increase human susceptibility to multiple autoimmune diseases and insufficient PD-1 signaling can lead to dysregulated T cell responses. Rosnilimab's activity is anticipated to modulate activated T cells and may be applicable to treatment of T cell-mediated human inflammatory diseases. Rosnilimab demonstrated *in vivo* efficacy in an animal model of inflammation and *ex vivo* inhibition of primary immune cells from alopecia areata patients. AnaptysBio anticipates initiation of a randomized placebo-controlled 45-patient Phase 2 trial of rosnilimab in moderate-to-severe alopecia areata, called AZURE, during the upcoming few months.

About AnaptysBio
AnaptysBio is a clinical-stage biotechnology company developing first-in-class antibody product candidates focused on unmet medical needs in inflammation. The Company's proprietary anti-inflammatory pipeline includes imsidolimab, its anti-IL-36R antibody, previously referred to as ANB019, for the treatment of dermatological inflammatory diseases, including generalized pustular psoriasis, or GPP, moderate-to-severe acne and moderate-to-severe hidradenitis suppurativa; rosnilimab, its anti-PD-1 agonist program, previously referred to as ANB030, for treatment of moderate-to-severe alopecia areata; and its BTLA modulator program, ANB032, which is broadly applicable to human inflammatory diseases associated with lymphoid and myeloid immune cell dysregulation. AnaptysBio's antibody pipeline has been developed using its proprietary somatic hypermutation, or SHM platform, which uses in vitro SHM for antibody discovery and is designed to replicate key features of the human immune system to overcome the limitations of competing antibody discovery technologies. AnaptysBio has also developed multiple therapeutic antibodies in an immuno-oncology collaboration with GSK, including an anti-PD-1 antagonist antibody (JEMPERLI (dostarlimab-gxly) GSK4057190), an anti-TIM-3 antagonist antibody (cobolimab, GSK4069889) and an anti-LAG-3 antagonist antibody (GSK4074386), and an inflammation collaboration with Bristol-Myers Squibb, including an anti-PD-1 checkpoint agonist antibody (CC-90006) currently in clinical development.

Forward-Looking Statements
This press release contains forward-looking statements within the meaning of the "safe harbor" provisions of the Private Securities Litigation Reform Act of 1995, including, but not limited to the timing of initiation of our Phase 2 clinical trial of rosnilimab in moderate-to-severe alopecia areata and the potential of rosnilimab to treat T cell-mediated human inflammatory diseases. Statements including words such as "plan," "continue," "expect," or "ongoing" and statements in the future tense are forward-looking statements. These forward-looking statements involve risks and uncertainties, as well as assumptions, which, if they do not fully materialize or prove incorrect, could cause our results to differ materially from those expressed or implied by such forward-looking statements. Forward-looking statements are subject to risks and uncertainties that may cause the company's actual activities or results to differ significantly from those expressed in any forward-looking statement, including risks and uncertainties related to the company's ability to advance its product candidates, obtain regulatory approval of and ultimately commercialize its product candidates, the timing and results of preclinical and clinical trials, the company's ability to fund development activities and achieve development goals, the company's ability to protect intellectual property and other risks and uncertainties described under the heading "Risk Factors" in documents the company files from time to time with the Securities and Exchange Commission. These forward-looking statements speak only as of the date of this press release, and the company undertakes no obligation to revise or update any forward-looking statements to reflect events or circumstances after the date hereof.

Contact:
Dennis Mulroy
AnaptysBio, Inc.
858-732-0201
dmulroy@anaptysbio.com

Source: AnaptysBio, Inc.