Sensei Biotherapeutics Presents Preclinical Data for SNS-101, a pH-Selective Anti-VISTA Antibody, at the Society for Immunotherapy of Cancer (SITC) 36th Annual Meeting

November 12, 2021

V-domain Ig-containing suppressor of T-cell activation (VISTA) is a novel immune checkpoint protein that has been recognized as an important potential immunotherapeutic target

Preclinical data demonstrate that SNS-101 selectivity binds the active form of VISTA induced by the low pH environment of a tumor, which could overcome the challenges of rapid target-mediated drug elimination in the blood

IND-enabling studies underway for SNS-101

Company to webcast VISTA science symposium with a leading thought leader, Professor Robert Schreiber, Ph.D., on Tuesday, November 16 at 4:00 p.m. ET

BOSTON, Nov. 12, 2021 (GLOBE NEWSWIRE) -- Sensei Biotherapeutics, Inc. (NASDAQ: SNSE), an immunotherapy company focused on the discovery and development of next generation therapeutics for cancer, today announced the first preclinical data for SNS-101, its anti-VISTA (V-domain Ig suppressor of T cell activation) product candidate. The data will be presented during a poster session on November 13, 2021, at the Society for Immunotherapy of Cancer's (SITC 2021) 36 th Annual Meeting in Washington, D.C. and virtually.

"VISTA has been recognized for years as an important immune checkpoint but has been difficult to drug due to its unique pH-dependent biology," said Robert Pierce, M.D. chief scientific officer of Sensei Biotherapeutics. "VISTA is primarily expressed on myeloid cells, a hub of immunosuppressive activity, and functions as a checkpoint exclusively under acidic conditions where it binds to its receptor, PSGL-1. Our scientific team has been evaluating VISTA for several years. Accordingly, we believe, the key to unlocking the power of this checkpoint lies with the development of an antibody that selectively binds the active form of VISTA that is only present within the low pH of the tumor microenvironment. At SITC, we are excited to share the preclinical data demonstrating that SNS-101 binds active VISTA with high affinity and significant selectivity (~600-fold increase at pH 6.0 versus 7.4)."

Dr. Pierce continued, "We are also encouraged by early *in vivo* evidence from a human VISTA knock-in mouse model showing improved immune responses, including the anticipated combination effect with anti-PD1 in a PD1 blockade responsive tumor model. We continue to expand on this research and are looking forward to sharing more *in vivo* data at a future medical conference. IND-enabling studies are already underway to evaluate the potential of SNS-101 to become a novel treatment for solid cancers, as both a monotherapy and in combination, that overcomes on-target/off-tumor toxicities seen today with other I/O approaches."

Preclinical data for SNS-101 are being presented in a poster (#228) titled: **"Antagonistic pH-selective VISTA antibody SNS-101 potentiates anti-PD-1/PD-L1-induced anti-tumor immunity."** A summary of data in the poster include:

- Preclinical data demonstrated that SNS-101 successfully blocked the interaction of VISTA with its PSGL-1 receptor, demonstrating high-affinity binding to low pH-VISTA sub-nanomolar affinity with exemplary (>600-fold) pH-selectivity vs. physiologic pH-VISTA.
- SNS-101, in combination with an anti-PD-1 inhibitor, led to superior anti-tumor activity compared to PD-1 alone.
- SNS-101 is a fully human IgG1 and has entered IND-enabling studies.

Sensei will host a virtual science symposium on Tuesday, November 16, 2021, at 4:00 p.m. Eastern Time to discuss the potential of the VISTA checkpoint inhibitor to address current limitations of immune checkpoint therapy. The event will be hosted by Sensei's management team and will include a presentation on VISTA biology by Robert Schreiber, Ph.D., the Andrew M. Bursky and Jane M. Bursky Distinguished Professor of Pathology and Immunology, Professor of Molecular Microbiology and co-leader of the tumor immunology program at the Siteman Comprehensive Cancer Center and Founding Director of the Center for Human Immunology and Immunotherapy Programs at the Washington University School of Medicine.

A live webcast of the symposium will be available under "Events & Presentations" in the Investors section of the company's website at www.senseibio.com. An archived replay will be available for approximately 90 days following the event.

About VISTA (V-domain Ig suppressor of T cell activation)

VISTA (B7-H5) is recognized as an important immune checkpoint regulator that is expressed primarily on myeloid cells, a hub of immunosuppressive activity, and acts via binding to its receptor on T-cells (PSGL-1) at sub physiologic pH. Disrupting the interaction of VISTA and its receptor on T-cells has been shown to enhance T-cell activation and tumor cell death. The VISTA-PSGL-1 T-cell checkpoint is activated under low pH conditions such as the tumor microenvironment. VISTA is found to be expressed in numerous cancer types and appears to be associated with PD-1 resistance.

The therapeutic hypothesis that Sensei believes differentiates its VISTA program is that an effective and safe inhibitory anti-VISTA antibody must demonstrate: (1) selective binding to the active form of VISTA (protonated/low pH) in order to avoid target mediated drug disposition and on-target/off-tumor effects; (2) effective inhibition of active VISTA's interaction with PSGL-1; and (3) Fc-mediated activation of tumor resident myeloid cells to facilitate conversion from an immunosuppressive to an immune-activating phenotype.

About SNS-101

SNS-101 is a potent, pH-dependent fully human monoclonal antibody designed to block the interaction of VISTA, a novel immune checkpoint that is

expressed primarily on myeloid cells, with its receptor, PSGL-1. Selectivity is achieved because SNS-101 targets the active (i.e., protonated) VISTA present in the low pH tumor microenvironment. SNS-101 was selected based on 1) the lack of significant binding to VISTA at physiologic pH (i.e., deprotonated VISTA in the blood), and 2) its high-affinity binding to active VISTA (pH 6.0), which yielded a > 600-fold selectivity. Based on the biochemical properties of SNS-101, Sensei anticipates tumor microenvironment selective activity for this preclinical product candidate. VISTA has been shown to be expressed in numerous tumor types, including non-small cell lung cancer (NSCLC).

About Sensei Biotherapeutics

Sensei Biotherapeutics is a biopharmaceutical company engaged in discovery, development, and delivery of next generation immunotherapies with an initial focus on treatments for cancer. Sensei has developed two unique approaches – its TMAb™ (Tumor Microenvironment Activated biologics) platform, comprising unique human monoclonal antibodies and alpaca derived nanobodies that are selectively active in the tumor microenvironment, and its ImmunoPhage™ platform that leverages bacteriophage to drive the generation of tumor antigen-specific immune responses. Using its TMAb platform, the company has developed SNS-101, an antibody-based therapeutic targeting an immune checkpoint gene that inhibits anti-tumor immune responses called V-domain Ig suppressor of T cell activation (VISTA). Using the ImmunoPhage platform, Sensei is developing a library of ImmunoPhage, called Phortress™, with multiple tumor-associated antigens to create a personalized, yet off-the-shelf cocktail approach for treating cancer patients. The platform is designed to enable efficient, scalable and cost-effective manufacturing to support all of Sensei's clinical programs. SNS-401-NG is an ImmunoPhage cocktail in preclinical development for the treatment of Merkel Cell Carcinoma. For more information, please visit www.senseibio.com, and follow the company on Twitter @SenseiBio and LinkedIn.

Cautionary Note Regarding Forward-Looking Statements

Any statements contained in this press release that do not describe historical facts may constitute forward-looking statements as that term is defined in the Private Securities Litigation Reform Act of 1995. These statements may be identified by words such as "believe", "expect", "may", "plan", "potential", "will", and similar expressions, and are based on Sensei's current beliefs and expectations. These forward-looking statements include expectations regarding the development of Sensei's product candidates and platforms, and the potential attributes and benefits of Sensei's TMAb technology and SNS-101. These statements involve risks and uncertainties that could cause actual results to differ materially from those reflected in such statements. Risks and uncertainties that may cause actual results to differ materially include uncertainties inherent in the development of therapeutic product candidates, such as preclinical discovery and development, conduct of clinical trials and related regulatory requirements, Sensei's reliance on third parties over which it may not always have full control, and other risks and uncertainties that are described in Sensei's Annual Report on Form 10-K filed with the U.S. Securities and Exchange Commission (SEC) on March 30, 2021 and Sensei's other Periodic Reports filed with the SEC. Any forward-looking statements speak only as of the date of this press release and are based on information available to Sensei as of the date of this release, and Sensei assumes no obligation to, and does not intend to, update any forward-looking statements, whether as a result of new information, future events or otherwise.

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