Vincerx Pharma Provides American Society of Hematology Annual Meeting 2022 Poster Highlights on Enitociclib in Multiple Tumor Types

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In a multiple myeloma (MM) preclinical study, antitumor efficacy was observed with enitociclib as a monotherapy and in combination with several anti-MM agents

Significant MYC downregulation was observed in patients with double-hit diffuse large B-cell lymphoma (DH-DLBCL) and other B-cell malignancies with a 30-mg dose level while maintaining a favorable safety profile

Clinical trial to evaluate enitociclib in combination with venetoclax and prednisone (NIH sponsored) anticipated to commence in Q1 2023

PALO ALTO, Calif., Dec. 12, 2022 (GLOBE NEWSWIRE) -- Vincerx Pharma, Inc. (Nasdaq: VINC), a biopharmaceutical company aspiring to address the unmet medical needs of patients with cancer through paradigm-shifting therapeutics, today announced two poster presentations of preclinical and clinical data on the Company's lead asset, enitociclib (also known as VIP152) at the 64 th American Society of Hematology (ASH) Annual Meeting 2022 and additional data-related updates in the enitociclib program.

Enitociclib is a potent and selective CDK9 inhibitor currently in clinical development. The small molecule inhibitor targets P-TEFb/CDK9 and has shown robust pathway modulation as well as efficacy and safety in several preclinical tumor models and in early phase clinical studies.

"We are excited with the progress we have made in our enitociclib program," said Ahmed Hamdy, M.D., Chief Executive Officer of Vincerx Pharma. "At ASH, we reported robust pathway modulation in MM cell lines and antitumor efficacy data in vivo. We also presented preliminary clinical data in patients with relapsed/refractory chronic lymphocytic leukemia (CLL) and Richter syndrome (RS), continuing to show that enitociclib 30 mg is more efficacious than 15 mg, and we have definitively showed that 15 mg does not modulate the target in patients."

Dr. Hamdy added, "We believe the potential paths forward for this program are promising, including studying enitociclib in combination given its favorable safety profile. Earlier this year, we established a partnership with the National Institutes of Health (NIH) to study enitociclib in combination with venetoclax and prednisone in MYC DLBCL, non-GCB DLBCL, and peripheral T-cell lymphoma. We will also look at studying enitociclib in combination with a BTK inhibitor in Q1 2023. Currently, patients with CLL receive multiple rounds of combination therapies only to relapse or stay on a BTK inhibitor for the rest of their lives. We believe that enitociclib in combination with a BTK inhibitor could drive patients into a deeper remission allowing them to stop treatment. The benefit of time-limited treatment is reducing unwanted toxicities and the potential for developing resistance mutations."

Dr. Wyndham Wilson, Head, Lymphoma Therapeutics Section and Senior Investigator of the Lymphoid Malignancy Branch, Center for Cancer Research at the National Cancer Institute, added, "The partnership with Vincerx brings together our shared level of expertise, and we are excited about the potential of this combination study of enitociclib with venetoclax and prednisone. The ability of these agents to inhibit multiple important survival pathways suggests this combination could show significant activity in aggressive B-cell lymphomas."

Dr. Aru Narendran, Professor at the departments of Oncology and Pediatrics at the University of Calgary further added, "The preclinical data presented at ASH demonstrated the efficacy of enitociclib as a monotherapy and in combination with anti-MM agents across a range of in vitro MM cell lines, as well as in vivo models of MM, which provide rationale and biological reasoning for further optimization studies of CDK9 inhibitors for clinical applications and early phase clinical studies to improve outcomes in MM. In addition, going forward, these findings also lay the foundation for further preclinical studies to examine the efficacy of enitociclib and combinations in other refractory hematological malignancies driven by similar oncogenic mechanisms, including high-risk pediatric leukemias."

Dr. Mazyar Shadman, M.D., Fred Hutchinson Cancer Center, Seattle, WA, USA, noted that, "Clinical data presented at ASH demonstrated evidence of monotherapy clinical activity in DH-DLBCL and a favorable safety profile across a range of B-cell malignancies. The favorable safety profile of enitociclib makes it a viable combination partner."

Key ASH 2022 Presentation Highlights:

Poster presentation titled, "Preclinical Study of Enitociclib, a Selective CDK9 Inhibitor, in Combination with Bortezomib, Lenalidomide, Pomalidomide, or Venetoclax in the Treatment of Multiple Myeloma", presented by Andy Son Tran, BSc, Department of Oncology, University of Calgary, AB, Canada, include:

- Enitociclib was identified as a top hit in small molecule inhibitor screening and exposure to enitociclib for 96 hours against a representative panel of MM cell lines (NCI-H929, MM.1S, OPM-2, and U266B1) demonstrated significant cytotoxic activity, with IC_{50} values ranging from 36 to 78 nM.
- Induction of apoptosis was observed with cleavage of pro-caspase-3 and PARP by western blotting in a time- and

dose-dependent manner with enitociclib as a single-agent, in addition to the depletion of phosphorylated RNAPII (Ser 2/5), MYC, MCL1, and PCNA proteins.

- Enitociclib synergizes with several anti-MM agents (bortezomib, lenalidomide, pomalidomide, and venetoclax [synergy scores >10]) at pharmacologically relevant concentrations across several MM cell lines.
- Enitociclib enhances the efficacy of lenalidomide and venetoclax as demonstrated by robust apoptosis induction through caspase-3 activation and PARP cleavage at 2 hours.
- In a JJN-3 MM xenograft mouse model, intravenous administration of enitociclib transiently inhibits the transcription of MYC and MCL1 and promotes apoptosis by induction of pro-caspase-3 and PARP cleavage with the onset of drug-induced effects seen as early as 1 hour after enitociclib treatment. Tumor volumes were reduced by 96% to 99% as compared with control mice on day 20 after the commencement of treatment. Increased efficacy of enitociclib in combination with lenalidomide was observed.
- Overall, these studies present evidence that enitociclib has significant antitumor activity against MM cell lines and provides specific pharmacologic targetability of several key oncogenic pathways involving proteins such as MYC, MCL1, and PCNA, leading to growth inhibition and apoptosis.

Poster presentation titled, “Enitociclib (VIP152/formerly BAY1251152) Is a Selective and Active CDK9 Inhibitor: Preliminary Safety and Early Signs of Efficacy in Patients with Non-Hodgkin Lymphoma (NHL) and Chronic Lymphocytic Leukemia (CLL)”, presented by Mazyar Shadman, M.D., Fred Hutchinson Cancer Center, Seattle, WA, USA, include:

- Updated clinical data on 20 patients, 16 NHL from study VNC-152-101 (NCT02635672) and 4 CLL patients from study VNC-152-102 (NCT04978779) were presented. Safety and preliminary efficacy data for 5 newly enrolled patients with MYC+ tumors (one each: DH-DLBCL, Richter syndrome [RS], transformed follicular lymphoma [tFL], Burkitt lymphoma, and mantle cell lymphoma [MCL]), in addition to the previously reported 11 patients, making a total of 16 NHL patients in VNC-152-101.
- Patients with NHL were heavily pretreated with >3 prior therapies with a median number of 4 enitociclib doses administered. As part of prior therapy, patients with CLL had received an approved BTKi, 3 patients had received venetoclax, and 2 patients had received CAR-T.
- Monotherapy treatment with enitociclib (doses of 10 to 30 mg) has a favorable safety profile in a pooled safety analysis for NHL/CLL (n=20) that is consistent with previously reported safety data:
    - Mainly Grade 1 and 2 gastrointestinal adverse events (AEs).
    - Neutropenia was observed in 8 patients with supportive care (G-CSF) administered to 3 patients.
    - There were no discontinuations due to an AE; 3 deaths due to disease progression.
- Enitociclib monotherapy treatment showed 1 stable disease (SD), 3 radiologic disease progression, and 1 clinical progression.
    - The patient with tFL with SD had a 16% reduction in tumor burden at the end of cycle 2 and at cycle 7 a 22% reduction in tumor burden (this patient is currently still on study); this response kinetics is consistent with the 2 previously reported DH-DLBCL patients who achieved SD at cycle 2 and metabolic CRs at cycle 10.
- Enitociclib does not inhibit T-cell dependent antibody response in a rat model.
    - AUC_{0-24} was 390 ng*hr/mL and 1820 ng*mg/mL following enitociclib doses of 0.33 mg/kg/week and 1.25 mg/kg/week, respectively.
    - The exposure observed for the 1.25 mg/kg group was comparable to the exposure observed in patients who received 30 mg enitociclib.
    - Results from this preclinical study suggests enitociclib is not expected to hamper vaccine response.
- In patients with NHL and CLL, enitociclib PK properties are comparable at the same dose (C_{max}, AUC_{0-t}) and across doses (CL, V_{SS} and $t_{1/2}$). Enitociclib PK are consistent with previously reported data in patients with NHL.
- Pharmacodynamic data show enitociclib 10/15 mg does not deliver adequate control of oncogenic signals of MYC, MCL1, and PCNA mRNA as compared with other NHL patients (MCL and DH-DLBCL) dosed at 30 mg.
    - The 30-mg dose of enitociclib is well-tolerated by patients with CLL/RS, consistent with observations of 30 mg in NHL/solid tumor indications.
    - Patients will CLL (n=2) treated with 10/15 mg did not respond to enitociclib, in line with the data showing that the 10/15-mg dose level does not appear to be able to deliver downregulation of MYC, MCL1 and PCNA mRNA.
    - In blood, the maximum extent of inhibition for MYC, MCL1, and PCNA mRNAs was 98%, 76%, and 92%, respectively. The maximal inhibition of all mRNAs in the blood occurred within 4 hours of enitociclib treatment in patients with DH-DLBCL and other B-cell malignancies (CLL, tFL, MCL, and Burkitt lymphoma) with the once weekly 30-mg dose of enitociclib.

Copies of the presentation materials can be accessed on the Investors section of the Company’s website at www.vincerx.com.

ABOUT VINCERX PHARMA, INC.

Vincerx Pharma, Inc. (Vincerx) is a clinical-stage life sciences company focused on leveraging its extensive development and oncology expertise to advance new therapies intended to address unmet medical needs for the treatment of cancer. Vincerx has assembled a management team of biopharmaceutical experts with extensive experience in building and operating organizations that develop and deliver innovative medicines to patients.

Vincerx's current pipeline derives from an exclusive license agreement with Bayer and includes a clinical-stage and follow-on small molecule drug program and a preclinical stage modular bioconjugation platform, which includes next-generation antibody-drug conjugates and innovative small molecule drug conjugates. For more information, please visit **www.vincerx.com**.

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This press release contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended (the "Securities Act"), and Section 21E of the Securities Exchange Act of 1934, as amended, that are intended to be covered by the "safe harbor" created by those sections. Forward-looking statements, which are based on certain assumptions and describe future plans, strategies, expectations and events, can generally be identified by the use of forward-looking terms such as "believe," "expect," "may," "will," "should," "would," "could," "suggest," "seek," "intend," "plan," "goal," "potential," "on-target," "on track," "project," "estimate," "anticipate" or other comparable terms. All statements other than statements of historical facts included in this press release are forward-looking statements. Forward-looking statements include, but are not limited to: Vincerx's business model, pipeline, strategy, timeline, product candidates and attributes and preclinical and clinical development and results. Forward-looking statements are neither historical facts nor assurances of future performance or events. Instead, they are based only on current beliefs, expectations and assumptions regarding future business developments, future plans and strategies, projections, anticipated events and trends, the economy and other future conditions. Forward-looking statements are subject to inherent uncertainties, risks and changes in circumstances that are difficult to predict and many of which are outside of our control.

Actual results, conditions and events may differ materially from those indicated in the forward-looking statements. Therefore, you should not rely on any of these forward-looking statements. Important factors that could cause actual results, conditions and events to differ materially from those indicated in the forward-looking statements include, but are not limited to: general economic, financial, legal, political and business conditions and changes in domestic and foreign markets; the potential effects of health epidemics and pandemics, including COVID-19; risks associated with preclinical or clinical development and trials, including conducted prior to Vincerx's in-licensing; failure to realize the benefits of Vincerx's license agreement with Bayer; risks related to the rollout of Vincerx's business and the timing of expected business milestones; changes in the assumptions underlying Vincerx's expectations regarding its future business or business model; Vincerx's ability to develop and commercialize product candidates; Vincerx's capital requirements and availability and uses of capital; the effects of competition on Vincerx's future business; the impact of Vincerx's workforce and cost reductions; and the risks and uncertainties set forth in Forms 10-K, 10-Q and 8-K most recently filed with or furnished to the SEC by Vincerx. Forward-looking statements speak only as of the date hereof, and Vincerx disclaims any obligation to update any forward-looking statements.

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