Immuneering Announces Positive Initial Phase 1 Pharmacokinetic, Pharmacodynamic and Safety Data for IMM-1-104 Universal-RAS Program; Accelerates Study Timeline

April 18, 2023

- *Data presented at AACR Annual Meeting support IMM-1-104's potential to address a broad population of patients with RAS mutant tumors*
- *IMM-1-104 well tolerated with no dose limiting toxicities (DLTs) or serious adverse events (SAEs) observed*
- *First demonstration of novel deep cyclic inhibition mechanism in humans, with IMM-1-104 achieving significant levels of PK C_{max} and a half-life of approximately two hours as predicted*
- *Pharmacodynamic data support potential to evaluate preliminary efficacy sooner than expected*
- *Study timeline accelerated: recommended Phase 2 dose (RP2D) now expected in early 2024*
- *Investor call to be held today at 9.00 a.m. ET*

CAMBRIDGE, Mass., April 18, 2023 (GLOBE NEWSWIRE) -- Immuneering Corporation (Nasdaq: IMRX), a clinical-stage oncology company developing medicines for broad populations of cancer patients with an initial aim to develop a universal-RAS therapy, announced positive initial pharmacokinetic (PK), pharmacodynamic (PD) and safety data from the Phase 1 trial of IMM-1-104 (NCT05585320), which are being shared today in a poster presentation titled “Humanized 3D tumor models that are mutationally aligned with AACR GENIE patients predict IMM-1-104 activity in RAS-addicted tumors” (abstract #4265) at the American Association for Cancer Research (AACR) annual meeting.

“We are very pleased to share initial PK, PD and safety data from our Phase 1 trial of IMM-1-104 in patients with advanced RAS mutant solid tumors, ahead of schedule,” said Ben Zeskind, Ph.D., MBA, Co-founder, and Chief Executive Officer of Immuneering. “We believe these data from the first patients dosed in our study demonstrate the PK, PD and safety profile necessary for deep cyclic inhibition – the proprietary and novel mechanism through which our therapies are designed to selectively impact cancer cells to a greater extent than healthy cells, regardless of the specific RAS mutation driving the tumor. The data show that we were able to reach significant levels of PK C_{max} with the aim of breaking tumor addiction to the MAPK pathway, then rapidly clearing out drug with IMM-1-104’s short half-life. These results position us to accelerate the dose escalation portion of our study, reaching potentially therapeutic levels of IMM-1-104 earlier than previously planned.”

“These initial PK and PD Phase 1 data with IMM-1-104 mark a major milestone for Immuneering, and for patients affected by RAS mutant tumors. It is the first time IMM-1-104 has shown the profile we believe is necessary for deep cyclic inhibition in humans. Prior therapies have often suffered from steep increases in drug half-life in humans when compared to preclinical models. In contrast, initial clinical results for IMM-1-104 are in line with our preclinical modeling, which we believe helps to de-risk an important element of our universal-RAS program,” said Brett Hall, Ph.D., Chief Scientific Officer of Immuneering. “With today’s results showing an approximate two-hour half-life coupled with reaching target C_{max} values faster than expected plus encouraging pharmacodynamic, safety and tolerability results observed, we are accelerating the remaining dose-escalation portion of our trial. We now have an opportunity to assess potential preliminary efficacy earlier than anticipated.”

“We are highly encouraged by the initial safety and tolerability data generated to date. IMM-1-104 has been well tolerated with no DLTs or SAEs observed,” said Scott Barrett, M.D., Chief Medical Officer of Immuneering. “We are grateful to the patients participating in our trial, and to the investigators. Investigator enthusiasm remains high, which combined with our study’s broad inclusion criteria, gives us confidence in our ability to keep enrolling patients in an expeditious manner.”

The Phase 1/2a clinical trial is an open-label study designed to evaluate the safety, tolerability, PK and preliminary efficacy of IMM-1-104 in patients with advanced RAS mutant solid tumors. The Phase 1 portion of the study, which is being conducted at five clinical sites in the United States, is evaluating IMM-1-104 following a Bayesian mTPI-2 escalation design, which includes a dose escalation phase and dose evaluation phase to establish an optimized RP2D candidate. Following selection of the RP2D candidate, the Company expects to conduct a Phase 2a dose expansion phase to assess the safety and efficacy of IMM-1-104 at the RP2D in RAS mutated pancreatic, melanoma, lung and colorectal cancers.

Highlights of the initial IMM-1-104 Phase 1 PK, PD and safety data presented at AACR include (as of data cut-off date of April 10, 2023, including patients with pancreatic and colon cancer):

- Significant PK C_{max} levels (plasma concentration of therapy in a specific area of the body) observed with IMM-1-104 of over 2,000 ng/mL (or approximately 1 uM drug free-fraction at 160 mg once daily oral dose)
- Greater than 90 percent PD inhibition of phosphorylated extracellular signal-regulated kinase (pERK) with IMM-1-104 compared to pretreatment baseline for patients at the third dose level (160 mg once daily oral)
- A median plasma half-life ($t_{1/2}$) of 1.94 hours observed with IMM-1-104 across the first three dose levels evaluable (40 mg, 80 mg and 160 mg once daily oral), in patients with pancreatic and colorectal cancer with different RAS mutations, including KRAS-G12D, the most common mutation present in pancreatic cancer
- IMM-1-104 was well tolerated with no DLTs or SAEs observed and no drug-related adverse events beyond Grade 1 observed

Based on the encouraging initial data presented today, Immuneering has updated guidance for the anticipated timing of announcing a RP2D for IMM-1-104 for its Phase 1/2a study. Management now expects to announce the RP2D in early 2024, versus prior guidance of mid-2024.

Other data presented at AACR:

In addition, IMM-1-104 was evaluated in humanized 3D preclinical tumor models displaying diverse mitogen-activated protein kinase (MAPK) pathway activation events. The MAPK pathway consists of a series of protein kinases such as RAS, RAF, MEK and ERK that are involved in many important cellular processes including cell proliferation, differentiation and survival. The antitumor activity of IMM-1-104 was evaluated in 132 tumor models spanning 12 distinct tumor types in a proprietary humanized 3D tumor growth assay (3D-TGA) conducted in Immuneering's labs in San Diego. Based on drug-response sensitivity and resistance profiles, a biomarker signature for IMM-1-104 was developed to project potential therapeutic response in more than 100,000 cancer patients found in the AACR Project GENIE® database. Mutational landscapes of patients within GENIE helped identify preclinical models that represent patient profiles likely to be encountered in the clinic. These results were utilized in prioritizing indications for the planned Phase 2a clinical trial.

Updated Near-Term Milestone Expectations

IMM-1-104

- Additional trial updates expected on a periodic basis.
- RP2D and additional safety data expected in early 2024.

IMM-6-415

- IND filing expected in the fourth quarter of 2023.

Conference Call

Immuneering will host a conference call and live webcast at 9:00 a.m. ET / 6:00 a.m. PT on April 18, 2023, to discuss the results and provide a business update. Individuals interested in listening to the live conference call may do so by using the webcast link in the "Investors" section of the company's website at www.immuneering.com. A webcast replay will be available in the investor relations section on the company's website for 90 days following the completion of the call.

About IMM-1-104

IMM-1-104 aims to achieve universal-RAS activity that selectively impacts cancer cells to a greater extent than healthy cells, through deep cyclic inhibition of the MAPK pathway with once-daily dosing. IMM-1-104 is currently being evaluated in a Phase 1/2a study in patients with advanced solid tumors harboring RAS mutations (NCT05585320).

About Immuneering Corporation
Immuneering is a clinical-stage oncology company developing medicines for broad populations of cancer patients with an initial aim to develop a universal-RAS therapy. The company aims to achieve universal activity through deep cyclic inhibition of the MAPK pathway, impacting cancer cells while sparing healthy cells. Immuneering's lead product candidate, IMM-1-104, is in a Phase 1/2a study in patients with advanced solid tumors harboring RAS mutations. The company's development pipeline also includes IMM-6-415, a universal-MAPK program, as well as several early-stage programs. For more information, please visit www.immuneering.com.

Forward-Looking Statements

This press release includes certain disclosures that contain "forward-looking statements," including, without limitation, statements regarding Immuneering's expectations regarding the treatment potential of IMM-1-104, the design, enrollment criteria and conduct of the Phase 1/2a clinical trial, the translation of preclinical data into human clinical data, the ability of initial clinical data to de-risk IMM-1-104 and be confirmed as the study progresses, including the safety, tolerability, pharmacokinetics, pharmacodynamics and potential efficacy of IMM-1-104; the potential advantages and effectiveness of the company's clinical and preclinical candidates, the timing of additional trial updates, recommended phase 2 dose and additional safety data, the indications to be pursued by Immuneering in the Phase 2a portion of the study, the timing of submission of the IND for IMM-6-415, and Immuneering's ability to advance its pipeline and further diversify its portfolio and make progress towards its longstanding goal of creating better medicines for cancer patients. Forward-looking statements are based on Immuneering's current expectations and are subject to inherent uncertainties, risks and assumptions that are difficult to predict. Factors that could cause actual results to differ include, but are not limited to, the risks inherent in oncology drug research and development, including target discovery, target validation, lead compound identification, lead compound optimization, preclinical studies, and clinical trials. These and other risks and uncertainties are described more fully in the section titled "Risk Factors" in Immuneering's most recent Form 10-K filed with the U.S. Securities and Exchange Commission. Forward-looking statements contained in this announcement are made as of this date, and Immuneering undertakes no duty to update such information except as required under applicable law.

Media Contact:
Gina Nugent
Nugent Communications
617-460-3579
gina@nugentcommunications.com

Investor Contacts:
Laurence Watts
Gilmartin Group
619-916-7620
laurence@gilmartinir.com

or

Kiki Patel, PharmD
Gilmartin Group
332-895-3225
kiki@gilmartinir.com