Immuneering Announces Positive Topline Results from Phase 1 Portion of its Phase 1/2a Clinical Trial of IMM-1-104 in RAS-Mutant Solid Tumors

March 14, 2024

- IMM-1-104 has been well-tolerated, demonstrating the potential for a differentiated safety profile -

- 100% suppression of acquired RAS alterations was observed in evaluable patients profiled for ctDNA and treated with IMM-1-104, supporting goal of Universal-RAS activity -

- Target lesion regression observed in over half of patients treated with IMM-1-104 at 320mg or 240mg QD, with best individual lesion regression of -35.7% and best RECIST sum of longest diameters (SLD) of -18.9%, both at 320mg -

- Candidate RP2D of 320 mg QD supported by tolerability, PK/PD, ctDNA results & initial anti-tumor activity -

- Phase 2a portion of the study underway with three monotherapy and two combination arms in earlier lines of treatment, with initial data from multiple arms expected in 2024 -

- Immuneering will host an investor call today at 8:30 a.m. ET. -

CAMBRIDGE, Mass., March 14, 2024 (GLOBE NEWSWIRE) -- Immuneering Corporation (Nasdaq: IMRX), a clinical-stage oncology company seeking to develop and commercialize universal-RAS/RAF medicines for broad populations of cancer patients, today announced positive topline results from the ongoing Phase 1 portion of its Phase 1/2a clinical trial of IMM-1-104 in advanced RAS-mutant solid tumors.

“Immuneering was founded with the goal of creating medicines for broad populations of cancer patients. In designing IMM-1-104, we sought to challenge the conventional wisdom that the MAPK pathway must be targeted narrowly and inhibited chronically, and that patients must often accept grueling toxicity. Insights from our platform led us to a fundamentally new approach, Deep Cyclic Inhibition, aiming to provide better tolerability and broader, universal-RAS activity,” said Ben Zeskind, Chief Executive Officer of Immuneering. “Today’s results are an important step towards that goal, as we share positive topline data from the Phase 1 portion of our Phase 1/2a clinical trial of IMM-1-104 in advanced RAS-mutant solid tumors. We believe these results demonstrate clear proof of concept, as IMM-1-104 shrank MAPK-dependent lesions in highly aggressive, late-line cancers, prevented acquired alterations in RAS, and has been well-tolerated, showing the potential for a differentiated safety profile.”

Ben Zeskind continued, “The endpoints of the Phase 1 portion were to assess the safety and tolerability of IMM-1-104, identify a candidate recommended Phase 2 dose (RP2D), and evaluate pharmacokinetics (PK). As of the data cut-off date of February 20, 2024, the patients in Phase 1 had a dozen different RAS mutations across eight different types of cancer. More than 60% of such patients had pancreatic cancer, more than 80% with available treatment history had never responded to any prior treatment for metastatic disease, and approximately two-thirds received IMM-1-104 in the third-line setting or later, up to seventh-line. IMM-1-104 has been well-tolerated and shown promising initial signs of clinical activity which we believe bodes well for the Phase 2a portion of our study; already underway and expected to enroll patients in earlier lines of treatment whose cancer has had less time to mutate. The Phase 2a portion is studying IMM-1-104 as a single agent and in combination, and could offer the clearest sign yet that IMM-1-104 has the potential to be an effective and universal treatment for RAS-mutant solid tumors. We expect to report initial data from multiple arms of our Phase 2a portion in 2024, and we look forward to sharing that data later this year.”

“Preliminary top line data from the Phase 1 portion of this trial with IMM-1-104 provided encouraging initial tumor activity and a well-tolerated safety profile in a refractory patient population,” said Vincent Chung, M.D., FACP, Professor, Department of Medical Oncology & Therapeutics Research at City of Hope, one of the largest cancer research and treatment organizations in the United States, and a principal investigator on this Phase 1/2a clinical study. “City of Hope looks forward to furthering clinical trials testing innovative, potentially lifesaving cancer treatments and will continue to evaluate IMM-1-104 in the Phase 2a portion of the study currently underway.”

Topline Results from IMM-1-104 Study Phase 1 Portion

Safety and Tolerability Results:

- As of February 20, 2024 (N=41), IMM-1-104 has been well-tolerated, with the potential for a differentiated safety profile.
- Among treatment-related adverse events (TRAEs) occurring in greater than 10% of patients, no grade 4 TRAEs were observed, only one grade 3 TRAE was observed (a non-serious rash that was reversible), and a modest number of grade 2 TRAEs were observed in each category. No TRAEs were deemed serious.

Deep Cyclic Inhibition Proof of Concept for IMM-1-104:

- As of February 20, 2024 (N=19), patient plasma data showed IMM-1-104 at 320mg inhibiting phosphorylated extracellular signal-regulated kinase (pERK) at a level of 90% or greater for 2.7 hours, before returning to near-zero levels in advance of 24 hours.
- IMM-1-104 at a 240mg dose achieved 90% or greater levels of pERK inhibition for 1.9 hours, before returning to near-zero levels in advance of 24 hours.

- Immuneering evaluated both 240mg and 320mg QD as prospective doses for the Phase 2a portion of its Phase 1/2a study. Based on data from this trial, Immuneering selected a candidate RP2D of 320mg QD.

Universal-RAS Proof of Concept for IMM-1-104:

- As of February 20, 2024 (N=22), 100% of evaluable patients profiled by ctDNA and treated with IMM-1-104 experienced no new acquired alterations in RAS.
- Excluding two patients treated with IMM-1-104 at 160mg (which Immuneering believes to be a sub-therapeutic dose), no new acquired alterations in MAPK pathway genes were observed, suggesting that there was no mutation in the MAPK pathway that a tumor could use to evade IMM-1-104.

Initial Signs of Clinical Activity:

While clinical activity was not an endpoint of the Phase 1 portion of the trial, Immuneering believes data generated as of the cutoff date of February 20, 2024 show promising signs for IMM-1-104's potential clinical activity:

- 53% of patients had ≥ 1 target lesion(s) regress when treated with IMM-1-104 at either 320mg or 240mg.
- Best individual lesion regressions were -35.7% at 320mg in second-line setting (vs. -11.4% at 240mg).
- Best RECIST SLD was -18.9% at 320mg in second-line setting (vs. -7.1% at 240mg).
- Longest duration on therapy was 162 days (5+ months) at 240mg, with no TRAEs.

"With the data from this trial through February 20, 2024, IMM-1-104 demonstrated its potential to induce Deep Cyclic Inhibition, and in doing so has been well tolerated – consistent with what we observed preclinically. We are also pleased with highly encouraging signs of activity observed among advanced RAS-mutant solid tumors," said Brett Hall, PhD., Chief Scientific Officer of Immuneering. "We have a growing group of enthusiastic investigators and sites who are commencing the Phase 2a trial. Today's clinical results would not have been possible without the investigators and patients participating in this study, to whom we extend our sincerest thanks, as well as the committed and hard work of my fellow Immuneers."

Immuneering plans to present further data from the ongoing Phase 1 portion of its Phase 1/2a study of IMM-1-104 in advanced RAS-mutant solid tumors at a future medical meeting.

Immuneering's Phase 1 portion of its 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 is being conducted at five clinical sites in the United States. Data from the Phase 1 portion led to Immuneering's candidate RP2D of 320mg for IMM-1-104. The Phase 2a portion is expected to include up to twenty clinical sites and has already dosed its first patient.

Near-Term Milestone Expectations

IMM-1-104

- Initial data from multiple arms of the Phase 2a portion of Immuneering's Phase 1/2a study of IMM-1-104 expected in 2024.

IMM-6-415

- First patient in Phase 1/2a trial of IMM-6-415 expected to be dosed in March 2024.

Conference Call

Immuneering will host a conference call and live webcast at 8:30 a.m. ET / 5:30 a.m. PT on March 14, 2024 to discuss the results and provide a business update. Individuals interested in listening to the live conference call may do so by dialing (800) 715-9871 for U.S callers and (646) 307-1963 for other locations and reference conference ID 7315708, or from 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 seeking to develop and commercialize universal-RAS/RAF 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 an oral, once-daily deep cyclic inhibitor currently in a Phase 1/2a study in patients with advanced solid tumors harboring RAS mutations. IMM-6-415 is an oral, twice-daily deep cyclic inhibitor being evaluated in a Phase 1/2a study in patients with advanced solid tumors harboring RAS or RAF mutations. The company's development pipeline also includes several early-stage programs. For more information, please visit www.immuneering.com.

Forward-Looking Statements

This press release contains forward-looking statements, including within the meaning of the Private Securities Litigation Reform Act of 1995. All statements contained in this press release that do not relate to matters of historical fact should be considered forward-looking statements, including, without limitation, statements regarding: Immuneering's plans to develop, manufacture and commercialize its product candidates; initial signs of clinical activity of IMM-1-104; the treatment potential of IMM-1-104; the design, enrollment criteria and conduct of the Phase 1/2a IMM-1-104 and IMM-6-415 clinical trials; the translation of preclinical data into human clinical data; the ability of initial and topline clinical data to de-risk IMM-1-104 and be confirmed as the study progresses, including the safety, tolerability, PK, pharmacodynamics and potential efficacy of IMM-1-104; the potential advantages and effectiveness of Immuneering's clinical and preclinical candidates; RP2D of IMM-1-104 and additional safety data; and the indications to be pursued by Immuneering in the Phase 2a portion of the IMM-1-104 trial and timing of results.

These forward-looking statements are based on management's current expectations. These statements are neither promises nor guarantees, but involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements, including, but not limited to, the following: the risks inherent in oncology drug research and development, including target discovery, target validation, lead compound identification, and lead compound optimization; we have incurred significant losses, are not currently profitable and may never become profitable; our projected cash runway; our need for additional funding; our unproven approach to therapeutic intervention; our ability to address regulatory questions and the uncertainties relating to regulatory filings, reviews and approvals; the lengthy, expensive, and uncertain process of clinical drug development, including potential delays in or failure to obtain regulatory approvals; our reliance on third parties and collaborators to conduct our clinical trials, manufacture our product candidates, and develop and commercialize our product candidates, if approved; failure to compete successfully against other drug companies; protection of our proprietary technology and the confidentiality of our trade secrets; potential lawsuits for, or claims of, infringement of third-party intellectual property or challenges to the ownership of our intellectual property; our patents being found invalid or unenforceable; costs and resources of operating as a public company; and unfavorable or no analyst research or reports.

These and other important factors discussed under the caption "Risk Factors" in our Annual Report on Form 10-K for the annual period ended December 31, 2023, and our other reports filed with the U.S. Securities and Exchange Commission, could cause actual results to differ materially from those indicated by the forward-looking statements made in this press release. Any such forward-looking statements represent management's estimates as of the date of this press release. While we may elect to update such forward-looking statements at some point in the future, except as required by law, we disclaim any obligation to do so, even if subsequent events cause our views to change. These forward-looking statements should not be relied upon as representing our views as of any date subsequent to the date of this press release.

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