Immuneering Presents Preclinical Data Demonstrating Encouraging Anti-Tumor Activity for IMM-1-104 and IMM-6-415 at AACR-NCI-EORTC Conference

October 12, 2023

– Expanded benchmarking of IMM-1-104 as a single agent across more than 190 patient-aligned models in humanized 3D-tumor growth assays demonstrated high sensitivity in a wide range of MAPK-driven tumor types, including models of RAS and RAF mutant melanoma, pancreatic cancer, and lung cancer

– IMM-1-104 in combination with gemcitabine or paclitaxel drove enhanced anti-tumor activity in humanized 3D-tumor growth assays across multiple pancreatic cancer models

– Strength of preclinical activity data together with encouraging tolerability results previously disclosed from the Phase 1a clinical trial provides strong rationale to evaluate IMM-1-104 in combination regimens while continuing to pursue a monotherapy strategy

– Benchmarking of IMM-6-415 as a single agent across more than 60 patient-aligned models in humanized 3D-tumor growth assays demonstrated high sensitivity in a wide range of MAPK-driven tumor types, including models of RAS and RAF mutant disease

– IMM-6-415 in combination with encorafenib drove deeper regressions and superior durability versus binimetinib plus encorafenib when compared head-to-head in animal models of RAF mutant melanoma and colorectal cancer; IND filing expected in 4Q 2023

CAMBRIDGE, Mass., Oct. 12, 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, today presented encouraging preclinical data for both IMM-1-104, its lead clinical-stage program, and IMM-6-415 at the AACR-NCI-EORTC International Conference on Molecular Targets and Cancer Therapeutics, taking place October 11-15, 2023 in Boston, Massachusetts.

"Today we are sharing new preclinical data that further support the potential of IMM-1-104 and IMM-6-415 as single agents and in combination regimens across a wide array of MAPK-driven tumor types, including those with RAS or RAF mutations," said Ben Zeskind, Ph.D., Co-founder and Chief Executive Officer of Immuneering. "Our goal is to help broad populations of cancer patients achieve better responses. The opportunity to advance our promising monotherapy programs while also targeting new opportunities in combination therapy could position us to develop safer and more effective treatment options for an even broader range of patients. Today's findings add cytotoxic agents and RAF inhibitors to the list of promising combinations, building on our previously disclosed data supporting combinations with KRAS-G12C inhibitors and immuno-oncology agents. Tolerability is important for successful combinations, and we designed IMM-1-104 and IMM-6-415 with a unique deep cyclic inhibition mechanism that aims to provide both good tolerability and broad activity in MAPK-driven tumors. We believe that IMM-1-104 and IMM-6-415, alone, and in combination with other agents, have the potential to bring significant benefit to broad populations of patients with RAS or RAF mutant cancers."

Details for the poster presentations are as follows:

Title: Predicting activity of IMM-1-104 as single agent and in combination for patients with RAS or RAF mutant tumors

- Anti-tumor activity of IMM-1-104 was characterized in 193 tumor models spanning 20 distinct tumor types in the humanized 3D-tumor growth assay (3D-TGA) using cancer-specific, patient-aligned cell lines.
- IMM-1-104 demonstrated diverse responses across a wide range of MAPK-driven tumor types, including those with RAS or RAF mutations.
- Pharmacogenomic data were used to generate a model predictive of response to IMM-1-104 and identify biomarker-aligned patient subpopulations.
- Sensitivity to IMM-1-104 (IC50 < 1uM) tested in 3D-TGA cell lines was highest in melanoma (62.5%) followed by pancreatic cancer (35.0%) and lung cancer (16.7%).
- IMM-1-104 was tested in combination with gemcitabine or paclitaxel in humanized 3D models of pancreatic cancer, demonstrating enhanced activity and combination therapy potential.
- IMM-1-104 in combination with encorafenib drove deeper regressions and superior durability of response in a head-to-head in vivo comparison versus binimetinib plus encorafenib. Tumor growth inhibition (TGI) was between 89.8% and 95.2% with the IMM-1-104 plus encorafenib combination and 73.7% with the binimetinib plus encorafenib combination.

Title: Deep Cyclic Inhibition of the MAPK pathway with IMM-6-415, alone and in combination with encorafenib, demonstrates anti-tumor activity and tolerability in RAF mutant tumors *in vivo*

- Anti-tumor activity of IMM-6-415 was evaluated in more than 60 humanized 3D-TGA models, which included 30 BRAF class I-mutant tumor models. Multiple drug-drug combinations have been explored, including vertical drug combinations with BRAF inhibitors.
- IMM-6-415, binimetinib and encorafenib were tested head-to-head as single agents and in combination with encorafenib in $BRAF^{V600E}$ melanoma and colorectal subcutaneous tumor xenograft models in female BALB/c nude mice.
- As monotherapy, IMM-6-415 demonstrated anti-tumor activity in over 50% (34 of 66) of the 3D-TGA models tested, including 30 BRAF mutant preclinical models in which 19 (63%) showed activity. Similar to IMM-1-104, resistant models either lacked an obvious MAPK pathway driver mutation or displayed parallel oncogenic activation events. Sensitive and intermediate responses were also strongly enriched for models harboring an activation mutation in RAS or RAF.
- Monotherapy treatment with encorafenib or IMM-6-415 displayed superior TGI when compared to binimetinib in the A-375 (melanoma) and HT-29 (colorectal) $BRAF^{V600E}$ tumor models.
- In combination with encorafenib, IMM-6-415 achieved a greater TGI *in vivo* than the combination of encorafenib plus binimetinib in $BRAF^{V600E}$ colorectal cancer and melanoma tumor models, suggesting an opportunity for IMM-6-415 as monotherapy or in combination regimens for the treatment of BRAF mutant tumors.

“In addition to RAS mutant disease, we are optimistic about the potential clinical translation and therapeutic potential for IMM-6-415 in RAF mutant disease,” said Brett Hall, Ph.D., Chief Scientific Officer of Immuneering. “Moreover, we believe IMM-6-415’s short half-life of approximately 20 minutes in mice, coupled with its superior preclinical activity compared to a currently available MEK inhibitor in RAF mutant models, may reinforce the opportunity for combination therapy of IMM-6-415 with RAF inhibitors in the clinic. We are also excited about the preclinical data we released today showing that IMM-1-104 can enhance the activity of cytotoxic agents that are currently used as standard of care treatment for pancreatic cancer patients in the first- or second-line setting.”

These abstracts are available on the AACR-NCI-EORTC International Conference on Molecular Targets and Cancer Therapeutics website. Posters will be available on the “Publications” section of Immuneering’s website at https://immuneering.com/publications.

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 oral dosing. IMM-1-104 is currently being evaluated in the Phase 1b dose expansion portion of a Phase 1/2a study in patients with advanced solid tumors harboring RAS mutations for whom there are limited treatment options (NCT05585320).

About IMM-6-415

IMM-6-415 targets RAF and RAS mutant tumors through deep cyclic inhibition of the MAPK pathway with an accelerated cadence. IMM-6-415 was designed with unique drug-like properties that distinguish it from other programs in the Immuneering pipeline, including a shorter half-life than IMM-1-104 which gives IMM-6-415 an accelerated cadence relative to the once-daily dosing of IMM-1-104. IMM-6-415 is being developed for monotherapy and combination applications in oncology, including the ability to enhance immune mediated therapy in certain settings. An IND filing for IMM-6-415 is expected in the fourth quarter of 2023.

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 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 concerning: the expected design, timing, enrollment and advancement of, and data results from, preclinical studies and clinical trials involving our product candidates; the potential of our product candidates to be used as monotherapies and / or in combination with other therapeutic agents, including to treat RAS or RAF mutant diseases; and the clinical development of IMM-1-104 and anticipated filing of an IND for IMM-6-415.

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 Quarterly Report on Form 10-Q for the quarterly period ended June 30, 2023, and our other reports filed with the United States 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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