



Immuneering Reports Data in Two Preclinical Abstracts at the ASCO 2022 Annual Meeting Highlighting Pan-KRAS/NRAS Activity of IMM-1-104

May 26, 2022

IMM-1-104 strongly inhibits tumor growth in an animal model of KRAS-G12V mutant pancreatic cancer

Preclinical data package now includes animal studies showing the potential for broad activity across tumors driven by MAPK pathway mutations including: KRAS-G12C, KRAS-G12D, KRAS-G12S, KRAS-G12V, NRAS-Q61R, and BRAF-V600E

IMM-1-104 IND expected in Q3 2022; Enrollment of the first patient in Phase 1 testing expected in Q4 2022

CAMBRIDGE, Mass., May 26, 2022 (GLOBE NEWSWIRE) -- Immuneering Corporation (NASDAQ: IMRX), a biopharmaceutical company using translational bioinformatics to advance a pipeline of product candidates designed to benefit large populations of patients with cancer and other diseases, today reported data in two preclinical abstracts at the 2022 ASCO Annual Meeting highlighting the pan-KRAS/NRAS activity of IMM-1-104. "These data underscore IMM-1-104's potential to broadly target solid tumors driven by a wide variety of frequently occurring KRAS and NRAS mutations. We believe IMM-1-104 focuses this pan-KRAS/NRAS activity selectively against malignant cells through its deep cyclic inhibition mechanism, which aims to deprive cancer cells of the sustained signaling they depend on to proliferate, while providing a cadenced release of inhibition that is designed to reduce the impact on healthy cells," said Ben Zeskind, Ph.D., MBA, chief executive officer of Immuneering Corporation. "We look forward to submitting our IND for IMM-1-104 in the third quarter of 2022 and enrolling our first patient in the Phase 1 trial in the fourth quarter of 2022."

The abstracts reported are as follows:

Head-to-head comparison of the dual-MEK inhibitor IMM-1-104 versus sotorasib or adagrasib in KRAS mutant pancreatic tumors.

Session Title: Gastrointestinal Cancer—Gastroesophageal, Pancreatic, and Hepatobiliary, publication only

Track: Gastrointestinal Cancer—Gastroesophageal, Pancreatic, and Hepatobiliary

First author: Peter King, Ph.D.

In this preclinical study, Immuneering researchers tested IMM-1-104 in a head-to-head comparison versus agents including sotorasib and adagrasib, in a series of preclinical models to characterize differential activity of each compound against pancreatic tumors driven by diverse KRAS mutations. Cell-based 2D biochemical and 3D growth assays were performed across nine pancreatic ductal adenocarcinoma (PDAC) models. The Capan-2 PDAC xenograft animal model was used to evaluate single agent activity of IMM-1-104 (75, 100, 150 mg/kg BID p.o. or 150 mg/kg QD p.o.) versus sotorasib or adagrasib (30 and 100 mg/kg QD p.o. each) for 21 days of treatment after tumors had reached volumes of 150 to 200 mm³.

The head-to-head comparison *in vivo* demonstrated a lack of Tumor Growth Inhibition (TGI) by sotorasib and adagrasib in KRAS-G12V mutant Capan-2 PDAC tumors. In contrast, IMM-1-104 observed TGIs of 49-84% across all doses and schedules tested. Consistent with other IMM-1-104 *in vivo* studies, median body weight loss was no more than 3-5% at top doses.

"These preclinical findings suggest that IMM-1-104 has the potential to offer a unique advantage over current therapeutic options for pancreatic cancers driven by a broad range of KRAS mutations that occur more commonly than KRAS-G12C," said Peter King, Ph.D., Vice President and Head of Discovery. "Our dual-MEK inhibitor has been designed to block pathway reactivation and have a short half life with the goal of achieving pan-KRAS/NRAS activity focused against malignant cells."

Translational modeling for patients with RAS mutant tumors: Profiling the dual-MEK inhibitor IMM-1-104 in a humanized 3D assay.

Session Title: Developmental Therapeutics—Molecularly Targeted Agents and Tumor Biology, publication only

Track: Developmental Therapeutics—Molecularly Targeted Agents and Tumor Biology

First author: Brett Hall, Ph.D.

In this preclinical study, Immuneering researchers characterized IMM-1-104's pharmacologic activity across 52 tumor cell lines that spanned 11 distinct tumor types in a humanized, Extracellular Matrix (ECM)-based 3D tumor growth assay (3D-TGA). Tumor models were categorized based on *in vivo* drug PK limits as sensitive to IMM-1-104 ($EC_{50} < 1 \mu M$), intermediate ($1 \mu M \leq EC_{50} \leq 10 \mu M$ and $\geq 25\%$ inhibition at $10 \mu M$), or resistant.

Models sensitive to IMM-1-104 were enriched for MAPK driver mutations, consistent with pathway addiction. Models with a MAPK

driver mutation and compensatory mutations such as PIK3CA or PTEN deletion were more likely to show intermediate response than those with a greater addiction to MAPK drivers. Models lacking a clear MAPK driver mutation but harboring other putative resistance alterations were more likely to be resistant in the 3D-TGA.

KRAS mutant pancreatic cancer and NRAS mutant melanoma were the most broadly sensitive patient-aligned models in the 3D-TGA and thus will be included among the target indications for Immuneering's planned Phase 1/2a clinical trial.

A copy of the abstracts can be accessed at: <https://meetings.asco.org/abstracts-presentations>

About Immuneering Corporation

Immuneering aims to improve patient outcomes by advancing a unique pipeline of oncology and neuroscience product candidates developed using its translational bioinformatics platform. Immuneering has more than a decade of experience applying translational bioinformatics to generate insights into drug mechanism of action and patient treatment response. Building on this experience, Immuneering's disease-agnostic discovery platform enables the company to create product candidates based on 1) biological insights that are both counterintuitive and deeply rooted in data, and 2) novel chemistry. Immuneering's lead product candidate IMM-1-104 aims to achieve pan-KRAS/NRAS activity that selectively impacts cancer cells to a greater extent than healthy cells. It is designed to be a highly selective dual-MEK inhibitor that further disrupts KSR to modulate the signaling dynamics of the MAPK pathway by driving deep cyclic inhibition that deprives tumor cells of the sustained proliferative signaling required for rapid growth, while providing a cadenced, moderate level of signaling sufficient to spare healthy cells. IMM-1-104 is being developed to treat advanced solid tumors in patients harboring RAS mutations, and is translationally guided by Immuneering's proprietary, human-aligned 3D tumor modeling platform combined with patient-aligned bioinformatics. In addition to IMM-1-104, Immuneering is evaluating its MEK-io product candidate, IMM-6-415, in IND-enabling studies, and has five other oncology programs in the discovery stage that are designed to target components of the MAPK or mTOR pathway, as well as two discovery stage neuroscience programs.

Forward-Looking Statements

This press release includes certain disclosures that contain "forward-looking statements," including, without limitation, statements regarding Immuneering's expectations the treatment potential of IMM-1-104 and IMM-6-415, the timing of submission of the IND and commencement of clinical trials for IMM-1-104 and IMM-6-415, the target indications of Immuneering's planned Phase 1/2a trial, 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 and neuroscience drug 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-Q 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.

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