Publication in Cancer Research Details Atebimetinib's Broad, Durable Preclinical Activity and Favorable Tolerability Across RAS- and RAF-Mutant Tumors via Deep Cyclic Inhibition

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- Atebimetinib showed broad antitumor activity across KRAS-, NRAS-, and BRAF-mutant models, including colorectal, lung, and melanoma, by resisting the RAF-mediated bypass signaling that has constrained other MEK inhibitors -

- In head-to-head in vivo studies, atebimetinib produced deeper, more durable tumor growth inhibition than the FDA-approved MEK inhibitor binimetinib -

- Atebimetinib was associated with favorable tolerability in preclinical models, consistent with Deep Cyclic Inhibitor technology's design to decouple antitumor activity from the toxicity of continuous MAPK suppression -

- In a preclinical cancer cachexia model, atebimetinib-treated animals sustained body weight near baseline through approximately two weeks of dosing, while untreated controls lost a median of more than 20% of body weight -

NEW YORK, July 21, 2026 (GLOBE NEWSWIRE) -- Immuneering Corporation (Nasdaq: IMRX), a late-stage clinical oncology company focused on keeping cancer patients alive and helping them thrive, today announced the publication of new findings in *Cancer Research*, a leading peer-reviewed journal of the American Association for Cancer Research, characterizing the differentiated mechanism and broad preclinical activity of atebimetinib.

The article, *"Dual-MEK Inhibitor Atebimetinib Displays Broad Activity in RAS- and RAF-Mutant Tumors via Deep Cyclic Inhibition and Resisting RAF-Bypass,"* (Kolitz et al., *Cancer Research*, doi.org/10.1158/0008-5472.CAN-25-4907) reports that atebimetinib demonstrated broad antitumor activity across RAS- and RAF-mutant models while resisting RAF-mediated bypass signaling, a key mechanism associated with resistance to other MEK inhibitors. Because the activity observed spanned a range of KRAS, NRAS, and BRAF alterations, the findings support the potential of atebimetinib to address RAS- and RAF-mutant cancers broadly — including the majority of RAS-mutant tumors that are not addressed by currently available mutation-selective inhibitors.

"Atebimetinib was deliberately designed to overcome the historical limitations of MEK inhibition, including the toxicity that comes with chronic MAPK pathway suppression, and the RAF-mediated pathway reactivation that has limited the durability of pathway suppression, particularly in RAS-mutant disease," said Brett Hall, Ph.D., Chief Scientific Officer of Immuneering. "The new findings noted in the *Cancer Research* article underscore the scientific basis for our Deep Cyclic Inhibitor technology and the broad, mutation-agnostic, durable activity we observed across RAS- and RAF-mutant models, reinforcing atebimetinib's position as a differentiated, modern MEK inhibitor."

The article describes how atebimetinib combines a novel dual-MEK mechanism with a short half-life designed to achieve Deep Cyclic Inhibition (DCI) of the MAPK pathway. Unlike other MEK inhibitors that chronically suppress signaling and are prone to RAF-mediated bypass, atebimetinib was shown to produce profound but transient inhibition of MAPK signaling followed by recovery periods that allow normal tissue to rest between doses – an approach designed to improve tolerability while maintaining antitumor activity.

Key findings include:

- Atebimetinib demonstrated potent inhibition of both pERK and pMEK across multiple KRAS-, NRAS-, and BRAF-mutant tumor models, including colorectal, lung, and melanoma models.
- Whereas other MEK inhibitors reduced pERK but allowed pMEK to accumulate — the molecular signature of RAF-mediated pathway reactivation — atebimetinib reduced both pERK and pMEK, reflecting its resistance to CRAF-mediated bypass.
- Atebimetinib's short half-life enabled deep cyclic inhibition of the MAPK pathway, characterized by deep suppression during peak exposure followed by recovery toward physiologic baseline signaling between doses.
- In multiple head-to-head *in vivo* studies, atebimetinib demonstrated greater depth and durability of tumor growth inhibition than the FDA-approved MEK inhibitor binimetinib across KRAS-, NRAS-, and BRAF-mutant tumor models while remaining well tolerated.
- In the Colon-26 model, a syngeneic colon-carcinoma model widely used to study cancer cachexia, atebimetinib-treated animals maintained body weight near baseline (within approximately 5%) through roughly two weeks of dosing, while untreated control animals lost a median of more than 20% of body weight by approximately day 14. Across the *in vivo*

models more broadly, atebimetinib-treated mice maintained body weight within a median of 3-5% over up to four weeks of chronic dosing.

Immuneering is currently recruiting patients in MAPKeeper 301 (NCT07562152), a global randomized Phase 3 pivotal trial evaluating atebimetinib plus mGnP versus standard-of-care gemcitabine/nab-paclitaxel in first-line metastatic pancreatic cancer. In the second half of the year, the company expects to dose the first patient in a Phase 2 trial of atebimetinib plus Libtayo® (cemiplimab) in patients with first-line RAS-mutant non-small cell lung cancer.

About Immuneering
Immuneering is a late-stage clinical oncology company dedicated to keeping cancer patients alive and helping them thrive, with an initial focus on patients with RAS, RAF, and other MAPK-driven cancers. The Company is developing an entirely new category of cancer medicines, Deep Cyclic Inhibitors, designed to improve overall survival by three mechanisms: shrinking tumors durably with less resistance, preserving body mass by countering cachexia, and minimizing side effects to maximize performance status and combinability. Immuneering's lead product candidate, atebimetinib, is an investigational, oral, once-daily Deep Cyclic Inhibitor of MEK, designed to improve survival across many cancer indications. The company is conducting a global randomized pivotal trial, MAPKeeper 301, evaluating atebimetinib in combination with chemotherapy in first-line pancreatic cancer patients. The Company's development pipeline also includes additional combination opportunities and preclinical 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: the treatment potential of atebimetinib, alone or in combination with other agents to treat cancer, including modified Gemcitabine/nab-paclitaxel (mGnP) in first-line pancreatic cancer and its potential to deliver overall survival with both durability and tolerability; the timing of dosing of the MAPKeeper 301 study and the Phase 2 study in combination with Libtayo®; the ability of the three design mechanisms of atebimetinib to shrink tumors durably, improve overall survival and overcome the limitations of conventional MAPK inhibition and provide a more sustained clinical benefit for patients.

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 activating trial sites or enrolling trial participants, 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 period ended December 31, 2025, 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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