

- Preclinical Combination Data Suggests Extra-Ordinary Synergy Between Certain DHODH Inhibitors and Nucleoside Analogues -

- Combination of IMU-838 and N4-Hydroxycytidine Reduced SARS-CoV-2 Virus Levels, Including the Delta Variant, Down to the Detection Limit -

NEW YORK and GOETTINGEN, Germany, Sept. 22, 2021 [PRNewswire/](#) -- **Immunic, Inc.** (Nasdaq: IMUX), a clinical-stage biopharmaceutical company developing a pipeline of selective oral immunology therapies focused on treating chronic inflammatory and autoimmune diseases, today announced the execution of an in-license agreement with the University Medical Center Goettingen, Germany, covering the combination of DHODH inhibitors and nucleoside analogues to treat viral infections (COVID-19 and Influenza). Terms of the agreement were not disclosed.

Preclinical research recently completed by the parties and their collaborators^[1] has shown that certain DHODH inhibitors, including Immunic's lead asset, IMU-838, strongly synergize with selected nucleoside analogues to inhibit SARS-CoV-2 replication *in vitro*. For instance, in an *in vitro* test system, IMU-838 alone showed an up to 99.9% reduction in viral RNA at concentrations of 5 µM, which is well within the exposure levels seen in prior clinical trials. Likewise, N4-hydroxycytidine (NHC), the active metabolite of molnupiravir^[2], alone, was associated with an up to 99% reduction in viral RNA at concentrations of 100 nM. Compared to single agent activity, the combination of IMU-838 and NHC achieved an extra-ordinary reduction in viral RNA, down to the limit of detection, reducing SARS-CoV-2 RNA by up to seven log units (corresponding to 0.00001% viral RNA remaining). This powerful reduction of virus replication *in vitro* was demonstrated across multiple SARS-CoV-2 variants, including alpha, beta and delta, highlighting the independence of this approach to mutant virus forms. In addition to molnupiravir, Immunic is exploring alternate nucleoside analogues, some of which have shown very promising antiviral activity *in vitro*. The company plans to present detailed data at an upcoming scientific conference.

"Research by the University Medical Center Goettingen and other research partners revealed a profound degree of synergy *in vitro* when combining certain nucleoside analogues with DHODH inhibitors, including both our lead asset IMU-838 and other of our preclinical molecules," stated Daniel Vitt, Ph.D., Chief Executive Officer and President of Immunic. "Recalling IMU-838's clinical activity against COVID-19 in our phase 2 CALVID-1 trial published earlier this year, and in light of recent exacerbations in COVID-19, worldwide, we are very excited to have in-licensed this technology to incorporate into our pandemic preparedness effort. However, with the extra-ordinary wealth of activity already ongoing at the company in other programs, we intend to evaluate and pursue the best possible strategic option for this program, including potential partnership, collaboration or external funding."

The company re-iterates its prior guidance that phase 2 top-line data of IMU-838 in ulcerative colitis is expected to be available in the second quarter of 2022, and that regarding IMU-935, data from the multiple ascending dose part of the ongoing phase 1 trial is expected in the fourth quarter of 2021, with initial clinical data in psoriasis expected in the second quarter of 2022. The phase 1 trial of IMU-935 in metastatic castration-resistant prostate cancer is expected to commence in the fourth quarter of 2021. Moreover, the company continues to expect enrollment of the first patient in the phase 2 CALLIPER trial of IMU-838 in progressive multiple sclerosis later this month, and first patient in the phase 3 ENSURE program of IMU-838 in relapsing-remitting multiple sclerosis in the fourth quarter of 2021.

Hella Kohlhof, Ph.D., Chief Scientific Officer of Immunic, commented, "We are very excited to see this remarkable synergistic antiviral activity, particularly as it is found well within exposure levels for IMU-838 in humans, associated with an extremely favorable safety profile. In addition to IMU-838, we also have a number of preclinical compounds that we believe are worth pursuing here, and we look forward to further refining potential combinations and compounds, with the goal of improving on the already strong antiviral activity demonstrated by IMU-838 alone in the clinic. We believe that this combination approach provides the most promising avenue for targeting potential future pandemics for many reasons, including the fact that, by focusing on the host cell-based mechanism, it should be insulated from many of the risks posed by viral resistance and the development of new strains."

Matthias Dobbstein, M.D., Professor of Molecular Oncology, University Medical Center Goettingen, added, "We are proud of the results of our preclinical work. These results identify a potential therapeutic strategy to inhibit the replication of SARS-CoV-2 in infected individuals. The synergistic antiviral effects of these combinations were astounding, and we are not aware of any other approaches which match this level of synergy against coronaviruses *in vitro*. We were very pleased with this license agreement with Immunic and look forward to future results with these very promising combinations."

[1] Immunic would like to thank its research partners, including Prof. Dr. med. Matthias Dobbstein, University Medical Center Goettingen, Jr.-Prof. Dr. Stephanie Pfänder, Ruhr-University Bochum, Prof. Dr. rer. nat. Manfred Marschall, Universitätsklinikum Erlangen, Brett L. Hurst, Ph.D., Utah State University, and MBM ScienceBridge GmbH.

[2] The nucleoside analogue which was most extensively studied in these tests was N4-hydroxycytidine (NHC), the active metabolite of molnupiravir, which is a drug candidate invented at Emory (DRIVE), LLC and licensed by Ridgeback Biotherapeutics, LP in collaboration with Merck & Co., Inc. (Europe: Merck Sharp & Dohme, or MSD) and which is currently in phase 3 development for COVID-19. Although the technology in-licensed by Immunic includes the potential combination of DHODH inhibitors with nucleoside analogues, including molnupiravir, Immunic does not have any rights to molnupiravir itself. As such, Immunic is currently focusing future research on combinations employing nucleoside analogues other than molnupiravir.

About IMU-838

IMU-838 is an orally available, next-generation selective immune modulator that inhibits the intracellular metabolism of activated immune cells by blocking the enzyme dihydroorotate dehydrogenase (DHODH). IMU-838 acts on activated T and B cells while leaving other immune cells largely unaffected and allows the immune system to stay functioning, e.g. in fighting infections. In previous trials, IMU-838 did not show an increased rate of infections compared to placebo. In addition, DHODH inhibitors, such as IMU-838, are known to possess a host-based antiviral effect, which is independent with respect to specific virus proteins and their structure. Therefore, DHODH inhibition may be broadly applicable against multiple viruses. IMU-838 was successfully tested in two phase 1 clinical trials in 2017 and is currently being tested in a phase 2 trial in patients with ulcerative colitis. In the third quarter of 2020, the company reported positive results from its phase 2 EMPHASIS trial of IMU-838 in relapsing-remitting multiple sclerosis, achieving both primary and key secondary endpoints with high statistical significance. In the first quarter of 2021, Immunic announced that IMU-838 showed evidence of clinical activity in its phase 2 CALVID-1 trial in hospitalized patients with moderate COVID-19. Also, in the first quarter of 2021, the company reported positive top-line data from an investigator-sponsored phase 2 proof-of-concept clinical trial of IMU-838 in primary sclerosing cholangitis which was conducted in collaboration with Mayo Clinic. To date, IMU-838 has been tested in more than 800 individuals and has shown an attractive pharmacokinetic, safety and tolerability profile. IMU-838 is not yet licensed or approved in any country.

About Immunic, Inc.

Immunic, Inc. (Nasdaq: IMUX) is a clinical-stage biopharmaceutical company with a pipeline of selective oral immunology therapies focused on treating chronic inflammatory and autoimmune diseases. The company is developing three small molecule products: its lead development program, IMU-838, a selective immune modulator that inhibits the intracellular metabolism of activated immune cells by blocking the enzyme DHODH and exhibits a host-based antiviral effect, is currently being developed as a treatment option for multiple sclerosis, ulcerative colitis, Crohn's disease, and primary sclerosing cholangitis. IMU-935, a selective inverse agonist of the transcription factor ROR γ t, is targeted for development in psoriasis, castration-resistant prostate cancer and Guillain-Barré syndrome. IMU-856, which targets the restoration of the intestinal barrier function, is targeted for development in diseases involving bowel barrier dysfunction. For further information, please visit: www.imux.com.

Immunic refers to Immunic, Inc. and/or its affiliates and subsidiaries.

Cautionary Statement Regarding Forward-Looking Statements

This press release contains "forward-looking statements" that involve substantial risks and uncertainties for purposes of the safe harbor provided by the Private Securities Litigation Reform Act of 1995. All statements, other than statements of historical facts, included in this press release regarding strategy, future operations, future financial position, future revenue, projected expenses, prospects, plans and objectives of management are forward-looking statements. Examples of such statements include, but are not limited to, statements relating to Immunic's three development programs and the targeted diseases; the potential for IMU-838 to safely and effectively target diseases; preclinical and clinical data for IMU-838; the timing of current and future clinical trials; the nature, strategy and focus of the company and further updates with respect thereto; and the development and commercial potential of any product candidates of the company. Immunic may not actually achieve the plans, carry out the intentions or meet the expectations or projections disclosed in the forward-looking statements and you should not place undue reliance on these forward-looking statements. Such statements are based on management's current expectations and involve risks and uncertainties. Actual results and performance could differ materially from those projected in the forward-looking statements as a result of many factors, including, without limitation, the COVID-19 pandemic, risks and uncertainties associated with the ability to project future cash utilization and reserves needed for contingent future liabilities and business operations, the availability of sufficient resources to meet business objectives and operational requirements, the fact that the results of earlier studies and trials may not be predictive of future clinical trial results, the protection and market exclusivity provided by Immunic's intellectual property, risks related to the drug development and the regulatory approval process and the impact of competitive products and technological changes. A further list and descriptions of these risks, uncertainties and other factors can be found in the section captioned "Risk Factors," in the company's Annual Report on Form 10-K for the fiscal year ended December 31, 2020, filed with the SEC on February 26, 2021, and in the company's subsequent filings with the Securities and Exchange Commission. Copies of these filings are available online at www.sec.gov or ir.imux.com/sec-filings. Any forward-looking statement made in this release speaks only as of the date of this release. Immunic disclaims any intent or obligation to update these forward-looking statements to reflect events or circumstances that exist after the date on which they were made. Immunic expressly disclaims all liability in respect to actions taken or not taken based on any or all the contents of this press release.

Contact Information

Immunic, Inc.

Jessica Breu
Head of Investor Relations and Communications
+49 89 2080 477 09
jessica.breu@imux.com

US IR Contact

Rx Communications Group
Paula Schwartz
+1-917-322-2216
immunic@rxir.com

US Media Contact

KOGS Communication
Edna Kaplan
+1 781 639 1910
kaplan@kogspr.com

SOURCE Immunic, Inc.

<https://ir.imux.com/2021-09-22-Immunic-and-the-University-Medical-Center-Goettingen-Sign-License-Agreement-Covering-the-Combination-of-DHODH-Inhibitors-and-Nucleoside-Analogues-to-Treat-Viral-Infections,-Including-COVID-19>