

- 30 mg and 45 mg Daily Doses of Vidofludimus Calcium Suppressed Development of Gadolinium-Enhancing Lesions by 78% and 74% Compared to Pooled Placebo at 24 Weeks –
- Improvements in Serum Neurofilament Light Chain Consistent with Recently Announced Interim Phase 2 CALLIPER Data in Progressive Multiple Sclerosis –
- Twin Phase 3 ENSURE Trials in Relapsing Multiple Sclerosis and Phase 2 CALLIPER Trial in Progressive Multiple Sclerosis Remain Underway –

NEW YORK, April 30, 2024 /PRNewswire/ -- **Immunic, Inc.** (Nasdaq: IMUX), a biotechnology company developing a clinical pipeline of orally administered, small molecule therapies for chronic inflammatory and autoimmune diseases, today announced that data from its phase 2 EMPHASIS trial of lead asset, vidofludimus calcium (IMU-838), in patients with relapsing-remitting multiple sclerosis (RRMS) has been published online on April 25, 2024 in *Neurology*® *Neuroimmunology & Neuroinflammation*, an official journal of the American Academy of Neurology.

The paper, lead authored by coordinating investigator, Robert J. Fox, M.D., Staff Neurologist, Mellen Center for Multiple Sclerosis, Vice-Chair for Research, Neurological Institute, Cleveland Clinic, Cleveland, Ohio, is entitled, "*Safety and Dose-Response of Vidofludimus Calcium in Relapsing Multiple Sclerosis: Extended Results of a Placebo-Controlled Phase 2 Trial.*" Dr. Fox receives consulting fees for serving as an advisor to Immunic. The paper can be accessed through the following link: <https://www.neurology.org/doi/full/10.1212/NXI.000000000200208>.

"The publication of our phase 2 EMPHASIS trial results for both study cohorts with an extended dose range in such a prestigious peer-reviewed journal represents further evidence of the strength of these findings for vidofludimus calcium in patients with RRMS," stated Daniel Vitt, Ph.D., Chief Executive Officer and President of Immunic. "As reported, a dose-dependent effect of vidofludimus calcium on the suppression of new combined unique active (CUA) magnetic resonance imaging (MRI) as well as gadolinium-enhancing (Gd+) lesions was demonstrated along with an encouraging initial signal towards reducing 12-week and 24-week confirmed disability worsening events as compared to placebo during the double-blind treatment period. The findings impressively underline the drug's combined neuroprotective and anti-inflammatory effects. Meanwhile, we continue to enroll patients in our twin phase 3 ENSURE trials in relapsing multiple sclerosis, from which we expect to report an interim futility analysis in late 2024, with the top-line readout of the first of the ENSURE trials anticipated in the second quarter of 2026."

Vidofludimus calcium, an orally available first-in-class nuclear receptor related 1 (Nurr1) activator and next-generation dihydroorotate dehydrogenase (DHODH) inhibitor, was shown to have suppressed MRI disease activity compared to placebo in patients with RRMS in the first cohort of the multicenter, double-blind, randomized, placebo-controlled phase 2 EMPHASIS trial, achieving all primary and key secondary endpoints with high statistical significance. The results of study cohort 1, exploring the doses of 30 mg and 45 mg of vidofludimus calcium in RRMS patients versus placebo, were published in *Annals of Clinical and Translational Neurology* in 2022 (Fox RJ, et al. *Ann Clin Transl Neurol.* 2022;9(7):977-987).

Given that both doses of 30 mg and 45 mg of vidofludimus calcium showed comparable robust activity on multiple endpoints, the trial enrolled an additional cohort of patients to receive a lower dose of vidofludimus calcium in order to further investigate a dose-response relationship by extending the trial to a broader dose range. Study cohort 2 explored the dose of 10 mg of vidofludimus calcium versus placebo. Extended results from the pooled EMPHASIS data (cohorts 1 and 2, including comparison to the pooled placebo group from both study cohorts) were summarized in more detail in this latest peer-reviewed article.

The pooled data showed that, compared to placebo, vidofludimus calcium suppressed the development of new CUA MRI lesions with daily doses of 30 mg and 45 mg up to week 24 by 76% and 71%, respectively. In addition, compared to placebo, vidofludimus calcium suppressed the development of Gd+ lesions with daily doses of 30 mg and 45 mg up to week 24 by 78% and 74%, respectively. Such robust anti-inflammatory effects were not seen with 10 mg, establishing 30 mg as the lowest effective dose. Serum neurofilament light chain (NfL), which is thought to correlate with neuronal destruction, decreased in a dose-dependent manner up to the highest tested dose of vidofludimus calcium by 9% (10 mg), 18% (30 mg) and 26% (45mg) compared to placebo, respectively, suggesting that the effect on NfL has a different dose-response pattern which contrasts with that observed with new CUA or Gd+ by MRI lesions.

Increases in disability over a pre-defined disability change threshold (defined as trigger events and measured by Expanded Disability Status Scale, EDSS) during the double-blind treatment period were confirmed after 12 or 24 weeks, designating them confirmed disability worsening (CDW) events. The number of patients who had confirmed 12- or 24-weeks CDW events was 3.7% for patients receiving placebo and only 1.6% for patients receiving any dose of vidofludimus calcium.

Finally, the pooled data set also reinforced that vidofludimus calcium was well-tolerated, in general, and that its safety profile was similar to the placebo group. Across cohorts 1 and 2, a total of 268 patients were randomized to 10 mg (n=47), 30 mg (n=71), or 45 mg (n=69) of vidofludimus calcium or placebo (n=81).

About Vidofludimus Calcium (IMU-838)

Vidofludimus calcium is a small molecule investigational drug in development as an oral next-generation treatment option for patients with multiple sclerosis and other chronic inflammatory and autoimmune diseases. The selective immune modulator activates the neuroprotective transcription factor nuclear receptor related 1 (Nurr1), which is associated with direct neuroprotective properties. Additionally, vidofludimus calcium is a known inhibitor of the enzyme dihydroorotate dehydrogenase (DHODH), which is a key enzyme in the metabolism of overactive immune cells and virus-infected cells. This mechanism is associated with the anti-inflammatory and anti-viral effects of vidofludimus calcium. Vidofludimus calcium has been observed to selectively act on hyperactive T and B cells while leaving other immune cells largely unaffected and enabling normal immune system function, e.g., in fighting infections. To date, vidofludimus calcium has been tested in more than 1,800 individuals and has shown an attractive pharmacokinetic, safety and tolerability profile. Vidofludimus calcium is not yet licensed or approved in any country.

About Immunic, Inc.

Immunic, Inc. (Nasdaq: IMUX) is a biotechnology company developing a clinical pipeline of orally administered, small molecule therapies for chronic inflammatory and autoimmune diseases. The company's lead development program, vidofludimus calcium (IMU-838), is currently in phase 3 and phase 2 clinical trials for the treatment of relapsing and progressive multiple sclerosis, respectively, and has shown therapeutic activity in phase 2 clinical trials in patients suffering from relapsing-remitting multiple sclerosis, progressive multiple sclerosis and moderate-to-severe ulcerative colitis. Vidofludimus calcium combines neuroprotective effects, through its mechanism as a first-in-class nuclear receptor related 1 (Nurr1) activator, with additional anti-inflammatory and anti-viral effects, by selectively inhibiting the enzyme dihydroorotate dehydrogenase (DHODH). IMU-856, which targets the protein Sirtuin 6 (SIRT6), is intended to restore intestinal barrier function and regenerate bowel epithelium, which could potentially be applicable in numerous gastrointestinal diseases, such as celiac disease, for which it is currently in preparations for a phase 2 clinical trial. IMU-381, which currently is in preclinical testing, is a next generation molecule being developed to specifically address the needs of gastrointestinal diseases. For further information, please visit: www.imux.com.

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, sufficiency of cash, expected timing, development and results of clinical trials, 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 development programs and the targeted diseases; the potential for vidofludimus calcium to safely and effectively target diseases; preclinical and clinical data for vidofludimus calcium; the timing of current and future clinical trials and anticipated clinical milestones; 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 substantial 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, increasing inflation, impacts of the Ukraine – Russia conflict and the conflict in the Middle East on planned and ongoing clinical trials, 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 financial and other resources to meet business objectives and operational requirements, the fact that the results of earlier preclinical studies and clinical 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, 2023, filed with the SEC on February 22, 2024, 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.

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<https://ir.imux.com/2024-04-30-Immunic-Announces-Publication-of-Extended-Data-From-Phase-2-EMPhASIS-Trial-of-Vidofludimus-Calcium-in-Relapsing-Remitting-Multiple-Sclerosis-in-the-Peer-Reviewed-Journal,-Neurology-R-Neuroimmunology-Neuroinflammation>