

Immunic Presents Key Vidofludimus Calcium Data at the 40th Congress of ECTRIMS, Highlighting Its Therapeutic Potential in Multiple Sclerosis

- Vidofludimus Calcium Consistently Reduced Neurofilament Light Chain Levels, Compared to Placebo, in the Interim Analysis of the Phase 2 CALLIPER Trial, Across Age and Disability Levels at Baseline For All Progressive Multiple Sclerosis Subtypes –*
- Clinical Signal Shown for Vidofludimus Calcium on Post COVID Fatigue May Be Related to Epstein-Barr Virus Reactivation; Preventing This Reactivation May Contribute to Fatigue Reduction in Multiple Sclerosis Patients –*
- Preclinical Data Showed Improved Neuronal Survival, Likely Driven by Vidofludimus Calcium’s Induction of Nurr1 Activation, as Demonstrated by Primary Target Gene Regulation –*
- In Preclinical Experiments, Vidofludimus Calcium Reduced or Prevented Development of Pathogenic Peripheral T Helper Cells, Which Could be One of the Treatment Pathways in Multiple Sclerosis –*

NEW YORK, September 18, 2024 – [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 the presentation of key data at the 40th Congress of the European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS), highlighting Immunic’s lead asset, nuclear receptor related 1 (Nurr1) activator, vidofludimus calcium’s (IMU-838) therapeutic potential in multiple sclerosis (MS). The data will be presented in an oral poster presentation and three ePosters at this conference, being held September 18-20, 2024, in Copenhagen, Denmark. Additionally, members of Immunic will be available throughout the event at booth #60.

“Having four poster presentations on our lead asset, vidofludimus calcium, at the prestigious ECTRIMS Congress, illustrates the strength of the data generated for our drug candidate, to date, and its potential to become a new treatment option for MS,” stated Daniel Vitt, Ph.D., Chief Executive Officer of Immunic. “We are particularly excited to have the opportunity to present data on various aspects of vidofludimus calcium’s profile, including the neurofilament light chain (NfL) interim data from our phase 2 CALLIPER trial, antiviral data suggesting an effect on reducing fatigue, Nurr1 target data supporting a neuroprotective profile, and pathogenic T cell data further supporting the drug’s anti-inflammatory effects.”

Dr. Vitt added, “As previously reported, in the interim analysis of our CALLIPER trial, we observed a clear separation from placebo in serum NfL levels among all patients with progressive multiple sclerosis (PMS) as well as its subtypes. These observations support the potential effectiveness of vidofludimus calcium in slowing disease progression in PMS and further substantiate its neuroprotective capabilities through the activation of Nurr1. Our next major data readout for this asset is the CALLIPER top-line data, which we expect to release in April of next year. We believe that, if the CALLIPER trial is successful in showing a beneficial effect of vidofludimus calcium, this data, along with that from the ENSURE program and vidofludimus calcium’s already established, strong safety and tolerability profile, may allow for a meaningful clinical differentiation of vidofludimus calcium compared to other MS medications, providing potentially attractive commercial positioning.”

Dr. Vitt continued, “Fatigue is one of the most common and most debilitating symptoms for both post-Covid Syndrome (PCS) and MS. Third-party research has recognized Epstein-Barr virus (EBV) reactivation as a potential cause for PCS fatigue. Notably, data has demonstrated not only vidofludimus calcium’s antiviral effects, but also its potential ability to prevent reactivation of EBV. We aim to confirm vidofludimus calcium’s potential to reduce fatigue in MS patients in our ongoing CALLIPER and phase 3 ENSURE trials and in the recently initiated investigator-sponsored phase 2 RAPID_REVIVE trial in PCS patients. Additionally, results from an animal model suggest that vidofludimus calcium reduces or prevents the development of pathogenic peripheral T helper cells. Besides its effect on pathogenic immune cells, preclinical evidence further suggests a neuroprotective role of vidofludimus calcium via activation of Nurr1. Preclinical data support Nurr1-driven direct neuroprotective effects by vidofludimus calcium enhancing neuronal survival and indirect effects by reducing neurotoxic activation of microglia cells. The combination of neuroprotective and anti-inflammatory effects of vidofludimus calcium represents a potential beneficial profile for effective treatment of MS.”

Oral Poster Presentation:

- **Title:** *Serum Neurofilament Changes in Progressive MS: Exploring the Impact of Vidofludimus Calcium by Age and Disability in the CALLIPER Study Interim Analysis*
- **Presenting Author:** Robert J. Fox, M.D., Staff Neurologist, Mellen Center for Multiple Sclerosis, Vice-Chair for Research, Neurological Institute, Cleveland Clinic, Cleveland, Ohio
- **Poster Number:** P753
- **Session Title:** Poster Session 2
- **Date:** Thursday, September 19, 2024
- **Time:** 4:45 pm – 6:45 pm CEST

In the phase 2 CALLIPER trial interim analysis of 203 patients, serum NfL levels were reduced by 22.4% ($p=0.01$, post hoc) after 24 weeks of vidofludimus calcium treatment compared to placebo, with consistent treatment effects across each progressive MS subtype, including primary progressive MS as well as active and non-active secondary progressive MS. The vidofludimus calcium group showed a 10% decrease in NfL versus a 20% increase for placebo among those with an Expanded Disability Status Scale (EDSS) score ≤ 5.5 ; and a 2% decrease for vidofludimus calcium versus a 12% increase for placebo among those with an EDSS score >5.5 . Similarly, among patients aged ≤ 45 years, the reduction was 11.6% for vidofludimus calcium versus a 15% increase for placebo, while for those aged > 55 years, it was a 10% decrease versus a 13% increase, respectively. The data suggest that vidofludimus calcium treatment consistently reduces NfL levels compared to placebo across different patient subgroups based on age and disability scores at baseline.

ePosters:

- **Title:** *Exploring the Potential of Vidofludimus Calcium to Reduce Fatigue in Multiple Sclerosis by Preventing Epstein-Barr Virus Reactivation*
- **ePoster Number:** P1119

Analysis of the antiviral activity of vidofludimus calcium *in vitro* revealed a dose-dependent reduction of lytic EBV reactivation in B cells and an anti-EBV effect in epithelial cells. Results of a post-hoc analysis of PCS symptoms in the phase 2 CALVID-1 trial indicated a potential contribution of vidofludimus calcium to the prevention of long-term fatigue. 80% of patients who received placebo reported fatigue compared to 50% who received 45 mg vidofludimus calcium. Fatigue decreased in both treatment groups in the next 9-17 weeks to 33% for placebo and 17% for vidofludimus calcium. A clinical signal for vidofludimus calcium

on PCS fatigue was observed which might be related to EBV reactivation. By preventing this reactivation, vidofludimus calcium may contribute to fatigue reduction in MS patients as well. This hypothesis will be further assessed by determining effects on fatigue using patient questionnaires as well as analyses of the anti-EBV effect in the ongoing CALLIPER, ENSURE, and RAPID_REVIVE clinical trials.

- **Title:** *Vidofludimus Calcium Activity on Nurr1 in Preclinical Models: A Potential Neuroprotective Function in Multiple Sclerosis*
- **ePoster Number:** P1410

Vidofludimus calcium enhanced the expression of Nurr1 target genes important for neuronal survival, such as brain derived neurotrophic factor (BDNF) and superoxide dismutase 1 (SOD1), in a rat neuronal cell line. Additionally, it upregulated key Nurr1 target genes, such as tyrosine hydroxylase (TH) and vesicular monoamine transporter 2 (VMAT2), in human microglial and murine neuronal cell lines, which could contribute to neuronal protection. Vidofludimus calcium protected neurons under pro-apoptotic conditions, reduced gene expression of IL-6, TNF α and IFN γ in human microglia stimulated with lipopolysaccharide (LPS), and increased BDNF levels in human peripheral blood mononuclear cells (PBMCs) stimulated with LPS. Vidofludimus calcium effectively attenuated disease severity in an experimental autoimmune encephalomyelitis (EAE) model. Treatment with vidofludimus calcium led to reduced immune cell infiltration, including decreased numbers of pathogenic T cells producing IL-17A, GM-CSF, and IFN γ . Preliminary data showed that mice receiving vidofludimus calcium exhibit elevated levels of BDNF in the blood and enhanced expression of Nurr1 and its target gene TH in the central nervous system.

- **Title:** *Vidofludimus Calcium Shows T Helper Cell Modulatory Effects in Murine Experimental Autoimmune Encephalomyelitis: One of the Potential Mode of Action Pathways for MS Treatment*
- **ePoster Number:** P1390

Vidofludimus calcium given prophylactically reduced disease severity and prevented disease development (63% and 15% symptom free in vidofludimus calcium and vehicle, respectively). This was reflected in the strong reduction of infiltrating T helper (Th) cells in the spinal cord as well as reduced numbers of proinflammatory Th cells in the periphery (draining lymph nodes, dLN). Vidofludimus calcium treatment, given after symptom onset, reduced disease progression compared to vehicle. This was supported by lower numbers of infiltrating proinflammatory Th cells into the spinal cord, while no significant difference was seen in the periphery compared to vehicle. The effect of vidofludimus calcium was assessed on myelin oligodendrocyte glycoprotein (MOG) antigen-specific Th cells (2D2) on day 7 after disease induction. Although vidofludimus calcium seems to increase MOG-specific follicular T helper (Tfh) cells in the periphery (dLN), the progression to develop into pathogenic Th cells was inhibited and the development of regulatory T cells was increased. Overall, vidofludimus calcium reduces or prevents development of pathogenic peripheral Th cells.

All poster presentations will be accessible on the "Events and Presentations" section of Immunic's website at: <https://ir.imux.com/events-and-presentations>.

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 and cash runway, 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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