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PureTech Health plc

**PureTech Health Announces Results from Two Studies of Tal Medical's LFMS Technology in Treatment-Resistant Major Depressive Disorder**

*Tal dose optimisation study showed consistent dose-dependent effect across multiple measurements but did not achieve statistical significance*

*Weill Cornell fMRI study demonstrated effects on brain activity in networks associated with depression*

Tal Medical, a clinical stage neuroscience company focused on the development of a non-invasive neuromodulation therapy and a subsidiary of PureTech Health (LSE: PRTC), today announced results from two studies evaluating Tal's proprietary Low Field Magnetic Stimulation (LFMS) technology in treatment-resistant major depressive disorder (TR-MDD). A Tal dose optimisation study did not meet statistical significance on its Hamilton Depression Rating Scale (HAM-D6) primary endpoint, although it showed a rapidly-acting, trending effect across multiple measurements in a dose-dependent manner. Separately, a functional magnetic resonance imaging (fMRI) study at Weill Cornell Medical College showed a reduction in functional connectivity in brain networks associated with depression after LFMS treatment.

"Given these latest results and the data from the RAPID trial reported in June, we will assess the utilisation of Tal resources and previously-earmarked PureTech cash and re-allocate as appropriate," said Daphne Zohar, PureTech Co-founder and CEO. "We will continue to analyse the full results from these studies in order to determine the best potential clinical application for this technology."

"Although we did not achieve statistical significance on the primary endpoint of our dosing study, the observed magnitude of the effect achieved in 2 to 4 days is on par with or higher than what antidepressant drugs typically achieve in 4 to 10 weeks and with a good safety profile," said Jan Skvarka, Tal Medical CEO. "We are considering several options to potentially increase the effect size and statistical power, including working with strategic partners and our trusted academic collaborators through non-dilutive sources."

"The data from both our dose ranging and Weill Cornell studies are encouraging and further suggest that LFMS has rapidly-acting effects on mood." said Steve Paul M.D., Tal Co-founder and Board Member. "Importantly, the dose-dependent effects of LFMS on self-rated as well as investigator-rated symptoms of depression seen in our dose ranging study, coupled with a highly favourable safety profile, support further work to optimise the LFMS field properties for the potential treatment of clinical depression."

This announcement contains inside information for the purposes of Article 7 of Regulation (EU) 596/2014.

**About the Dose Optimisation Study**

This study was designed to evaluate the effect of four consecutive daily sessions of 20 or 60 minutes of LFMS compared to sham treatment in subjects with TR-MDD (Week 1). In an exploratory Week 2 treatment consisting of another four consecutive daily sessions, Week-1 non-responders were randomised to receive either 120-minute LFMS or sham, while Week-1 responders were randomised to continue their Week-1 regimen or receive sham. All subjects were followed up for four weeks after the end of randomised treatment. 122 subjects were enrolled, and 120 completed Week 1 treatment and were included in the primary analysis. The primary analysis of baseline to endpoint change in HAMD6 showed a 1.0-point difference between active 60-minute LFMS and sham at the end of Week 1, though the difference was not statistically significant ( $p=0.31$ ). On MADRS, the study observed a 2.7-point difference, with a  $p$  value of 0.09 at the end of Week 1. Other secondary efficacy analyses showed a consistently trending, dose-dependent effect favouring LFMS over sham, with some analyses achieving a  $p$  value lower than 0.05 for the 60-minute arm in Week 1. No safety issues were identified during the study.

### **About the Weill Cornell fMRI Study**

The fMRI study at Weill Cornell was designed to evaluate the effect of LFMS on resting state functional connectivity within multiple brain networks related to depressive symptoms in subjects with TR-MDD. Symptoms were assessed using the 6-Item Hamilton Depression Rating Scale (HAMD6), Visual Analog Scale (VAS), and Positive and Negative Affect Schedule (PANAS) instruments. 66 subjects were enrolled, of whom 33 met the inclusion/exclusion criteria and were included in the per protocol analysis. The subjects underwent three 20-min LFMS treatments, as well as two fMRI imaging sessions (before and after the treatment regimen). In the per protocol sample, functional connectivity was reduced after active, but not sham, treatment in networks underlying negative rumination, attention and task performance. Several regions of functional connectivity change were statistically significant and specific to active-treatment responders. The per protocol sample also showed greater pre- to post-treatment reduction in the active LFMS vs sham group on HAMD-6 and VAS ( $p= 0.02$  and  $0.002$ , resp.), though no meaningful difference was observed on PANAS. In the intent-to-treat analysis, a greater pre- to post active vs sham treatment reduction was observed on VAS ( $p=0.02$ ), with no meaningful difference on HAMD6 and PANAS. Marc Dubin, M.D., Ph.D., Assistant Professor of Clinical Psychiatry and of Neuroscience in the Feil Family Brain and Mind Research Institute, and Director of Non-Invasive Brain Stimulation in the Department of Psychiatry at Weill Cornell Medicine was the study lead principal investigator.

### **About Tal Medical and Low Field Magnetic Stimulation**

[Tal Medical](#) is a clinical stage neuroscience company developing a non-invasive neuromodulation therapy for depression and other brain disorders. Tal's proprietary Low Field Magnetic Stimulation (LFMS) technology uses a unique magnetic field waveform, with a mechanism of action different from other brain stimulation techniques such as electroconvulsive therapy (ECT) or transcranial magnetic stimulation (TMS).

The previous proof-of-concept for LFMS was established at McLean Hospital in two randomised, sham-controlled studies focused primarily on bipolar depression. In those studies, a single 20-minute LFMS treatment demonstrated an immediate effect size greater than antidepressant drug treatments typically

achieve in 4-10 weeks. In June of this year, Tal and Massachusetts General Hospital (MGH) reported topline data from the RAPID study of LFMS in TR-MDD, in which treatment with LFMS did not achieve the primary endpoint of HAMD6 after two 20 minute sessions in core depression symptoms compared to sham treatment, though some non-statistically significant mood improvements were detected with active LFMS on the VAS instrument.

Tal Medical has an ongoing program in sleep along with several additional mechanistic studies.

Tal's Board of Directors includes Steve Paul, M.D., former president of the Lilly Research Laboratories of Eli Lilly and Company; Ben Shapiro, M.D., former Executive Vice President of Research for Merck and PureTech Health Non-Executive Director; Raju Kucherlapati, founder and former Board member of Abgenix (acquired by Amgen) and Millennium Pharmaceuticals (acquired by Takeda) and PureTech Health Independent Non-Executive Director; and Daphne Zohar, CEO and Co-founder of PureTech Health. Tal's Scientific Advisory Board includes Atul Pande, M.D., Former Senior Vice President, Head of Neuroscience and Senior Advisor, Pharmaceutical R&D at GlaxoSmithKline and PureTech Health Senior Advisor; Mark George, M.D., Layton McCurdy Endowed Chair, Distinguished Professor of Psychiatry, Radiology and Neuroscience and Director of the Brain Stimulation Laboratory at the Medical University of South Carolina; Maurizio Fava, M.D., Executive Vice Chair for the MGH Department of Psychiatry, Executive Director, MGH Clinical Trials Network and Institute (CTNI) and Director, MGH Depression Clinical and Research Program (DCRP); Robert Post, M.D., Former Chief of the Biological Psychiatry Branch at the National Institute of Mental Health (NIMH) and Professor of Psychiatry at George Washington University School of Medicine and Head of the Bipolar Collaborative Network in Bethesda, Maryland; and Hal Levine, D.O., EVP and Chief Medical Officer of Beacon Health Options.

PureTech Health plc (PRTC.L) has moved Tal Medical from Growth Stage to Project Phase. PureTech owns 54.2% of Tal on a diluted basis as of 30 June 2016. The ownership calculation includes issued and outstanding shares as well as options to purchase shares and written commitments to issue shares or options, but excludes unallocated shares authorised to be issued pursuant to equity incentive plans and any convertible debt.

### **About PureTech Health**

**PureTech Health** (PureTech Health plc, PRTC.L) is a cross-disciplinary biopharma company creating 21<sup>st</sup> century medicines that modulate the adaptive human systems. Our therapies target the immune, nervous, and gastro-intestinal systems by addressing the underlying pathophysiology of disease from a systems perspective rather than through a single receptor or pathway. We are advancing more than 20 clinical studies across our pipeline, with multiple human proof-of-concept studies and pivotal or registration studies expected to read out in the next two years. PureTech Health's rich and growing research and development pipeline has been developed in collaboration with some of the world's leading scientific experts, who along with PureTech's experienced team and board analyses more than 650 scientific discoveries per year to identify and advance the opportunities we believe hold the most promise for patients. This team and process place PureTech Health on the cutting edge of ground-breaking science

and technological innovation and leads the Company between and beyond existing disciplines. For more information, visit [www.puretechhealth.com](http://www.puretechhealth.com) or connect with us on [Twitter](#).

### **Forward Looking Statement**

This press release contains statements that are or may be forward-looking statements, including statements that relate to the company's future prospects, developments and strategies. The forward-looking statements are based on current expectations and are subject to known and unknown risks and uncertainties that could cause actual results, performance and achievements to differ materially from current expectations, including, but not limited to, those risks and uncertainties described in the risk factors included in the regulatory filings for PureTech Health plc. These forward-looking statements are based on assumptions regarding the present and future business strategies of the company and the environment in which it will operate in the future. Each forward-looking statement speaks only as at the date of this press release. Except as required by law and regulatory requirements, neither the company nor any other party intends to update or revise these forward-looking statements, whether as a result of new information, future events or otherwise.

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