# Jazz Pharmaceuticals Announces Top-line Results from Phase 3 Trial Evaluating Nabiximols Oromucosal Spray in Adult Participants with Multiple Sclerosis Spasticity

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*Nabiximols oromucosal spray continues to be evaluated in ongoing clinical trials in multiple sclerosis spasticity*

DUBLIN, June 28, 2022 /PRNewswire/ -- Jazz Pharmaceuticals plc (Nasdaq: JAZZ) today announced top-line results from the Phase 3 RELEASE MSS1 trial (NCT04657666) evaluating nabiximols oromucosal spray (JZP378, or Sativex ®, ex-U.S.) on clinical measures of spasticity in individuals with multiple sclerosis (MS). The RELEASE MSS1 trial did not meet the primary endpoint of change in Lower Limb Muscle Tone-6 (LLMT-6) between baseline and Day 21, as measured by the Modified Ashworth Scale (MAS).

Nabiximols oromucosal spray is a complex botanical mixture formulated from extracts of the cannabis sativa plant and contains the cannabinoids delta-9-tetrahydrocannabinol (THC) and cannabidiol (CBD), as well as other cannabinoid and non-cannabinoid components. Nabiximols oromucosal spray (known as Sativex ex-U.S. and first approved in the U.K. in 2010) has been approved in 29 countries for the treatment of adult patients with moderate to severe spasticity due to MS who have not responded adequately to other anti-spasticity medication based on previously completed clinical trials.

"We remain committed to the nabiximols program and are actively assessing the RELEASE MSS1 trial results, which will be presented at a future medical meeting. We look forward to additional data from two other ongoing trials that have the potential to support a U.S. FDA New Drug Application submission," said Rob Iannone, M.D., M.S.C.E., executive vice president, global head of research and development at Jazz Pharmaceuticals. "I would like to extend a heartfelt thank you to all those who supported and made this study possible, including the patients who were enrolled, their families, our investigators, staff, and all of the dedicated Jazz employees."

RELEASE MSS1 was the first, and smallest, of the three clinical trials in the current program, and it evaluated the safety and efficacy of nabiximols oromucosal spray in 68 patients with MS spasticity. Data from these trials will continue to be evaluated as it becomes available, to support the overall registrational program in the U.S. Two additional, ongoing Phase 3 trials to complement and inform a comprehensive development plan include:

- RELEASE MSS3: A Phase 3 multicenter, double-blind, placebo-controlled trial evaluating the efficacy of nabiximols oromucosal spray, compared to placebo, when added to standard of care, for the improvement of muscle spasms associated with MS over a 12-week treatment period. Estimated enrollment is 446 participants.
- RELEASE MSS5: A Phase 3 multicenter, randomized, double-blind, placebo-controlled, 2-treatment, 2-period, crossover trial evaluating the effect of multiple doses of nabiximols oromucosal spray compared to placebo on a clinical measure of velocity-dependent muscle tone in the lower limbs (Lower Limb Muscle Tone-6 [LLMT-6]) in participants with MS over a 3-week treatment period. Estimated enrollment is 190 participants.

The safety profile in RELEASE MSS1 was consistent with previously reported adverse events, with no new safety signals attributable to nabiximols oromucosal spray observed in this population.

Data from the RELEASE MSS1 trial will be submitted for presentation at a future medical meeting.

**About the RELEASE MSS1 Trial**

RELEASE MSS1 (NCT04657666) is a randomized, double-blind, placebo-controlled, two-way crossover trial that enrolled 68 adults with multiple sclerosis (MS) to evaluate the effect of nabiximols oromucosal spray on clinical measures of spasticity over a 3-week treatment period. After the trial initiated, the trial protocol was amended to provide flexibility on enrollment size. Ultimately, the initial intended number of patients was enrolled, and 68 patients were randomized. Participants entering the trial were over 18 years of age with a confirmed diagnosis of any disease subtype of MS for at least 12 months prior to first visit, were expected to remain stable for the duration of the trial and experienced spasticity not relieved by their current anti-spasticity medications.

Participants were randomized in a 1:1 ratio to one of two sequences comprised of treatment with nabiximols oromucosal spray and placebo. In the first period of the crossover trial, participants were titrated to a maintenance dose of nabiximols oromucosal spray or placebo in a blinded fashion; in the second period of the trial, participants then initiated therapy with the alternate study drug in a blinded fashion. The primary endpoint in RELEASE MSS1 was a measure of change from baseline in Lower Limb Muscle Tone-6 (LLMT-6) as defined by the Modified Ashworth Scale (MAS) at the end of each period, compared to placebo.

The secondary endpoints were change in Lower Limb Muscle Tone-4 (LLMT-4) as defined by the MAS, safety, and tolerability of nabiximols oromucosal spray, in individuals with MS spasticity.

**About Nabiximols Oromucosal Spray**

Nabiximols oromucosal spray is a complex botanical mixture formulated from extracts of the cannabis sativa plant. Nabiximols oromucosal spray contains the cannabinoids delta-9-tetrahydrocannabinol (THC) and cannabidiol (CBD), as well as other cannabinoid and non-cannabinoid components. Currently, there are no U.S. Food and Drug Administration (FDA) approved cannabis-derived medications that contain THC, and Epidiolex® is the only FDA approved cannabis-derived therapy.

Nabiximols oromucosal spray is indicated outside the U.S. as a treatment for symptom improvement in adult patients with moderate to severe spasticity due to multiple sclerosis (MS) who have not responded adequately to other anti-spasticity medications and who demonstrate clinically significant improvement in spasticity related symptoms during an initial trial of therapy. Nabiximols oromucosal spray is investigational and currently

not approved for any indication in the U.S.

**About Multiple Sclerosis Spasticity**

Multiple sclerosis (MS) spasticity is one of the most common motor syptoms associated with MS.[1] MS spasticity often manifests as involuntary muscle stiffness and/or spasms, occurring in up to 84 percent of individuals with MS, and approximately one-third of individuals with MS still live with uncontrolled spasticity symptoms.[2-4] However, MS spasticty can also lead to pain, sexual dysfunction, dysarthria, fatigue, depression and anxiety, mobility impairment, bladder and bowel dysfunction, and sleep disturbances.[2,5-7] Less than half of individuals with MS receiving treatment for spasticity are satisfied with the current treatment regimens[2] and 41 percent of physicians are dissatisfied with current treatment regimens.[8]

**About Jazz Pharmaceuticals plc**

Jazz Pharmaceuticals plc (Nasdaq: JAZZ) is a global biopharmaceutical company whose purpose is to innovate to transform the lives of patients and their families. We are dedicated to developing life-changing medicines for people with serious diseases – often with limited or no therapeutic options. We have a diverse portfolio of marketed medicines and novel product candidates, from early- to late-stage development, in neuroscience and oncology. Within these therapeutic areas, we are identifying new options for patients by actively exploring small molecules and biologics, and through innovative delivery technologies and cannabinoid science. Jazz is headquartered in Dublin, Ireland and has employees around the globe, serving patients in nearly 75 countries. For more information, please visit www.jazzpharmaceuticals.com and follow @JazzPharma on Twitter.

**Caution Concerning Forward-Looking Statements**

This press release contains forward-looking statements, including, but not limited to, statements related to nabiximols for people with MS spasticity and the potential impact on that community; the potential successful submission of a new drug application; and other statements that are not historical facts. These forward-looking statements are based on Jazz Pharmaceuticals' current plans, objectives, estimates, expectations and intentions and inherently involve significant risks and uncertainties. Actual results and the timing of events could differ materially from those anticipated in such forward-looking statements as a result of these risks and uncertainties, which include, without limitation, risks and uncertainties associated with: pharmaceutical product development; the regulatory approval process, and other risks and uncertainties affecting the company and its development programs, including those described from time to time under the caption "Risk Factors" and elsewhere in Jazz Pharmaceuticals plc's Securities and Exchange Commission filings and reports (Commission File No. 001-33500), including Jazz Pharmaceuticals' Annual Report on Form 10-K for the year ended December 31, 2021 and future filings and reports by Jazz Pharmaceuticals. Other risks and uncertainties of which Jazz Pharmaceuticals is not currently aware may also affect Jazz Pharmaceuticals' forward-looking statements and may cause actual results and the timing of events to differ materially from those anticipated. The forward-looking statements herein are made only as of the date hereof or as of the dates indicated in the forward-looking statements, even if they are subsequently made available by Jazz Pharmaceuticals on its website or otherwise. Jazz Pharmaceuticals undertakes no obligation to update or supplement any forward-looking statements to reflect actual results, new information, future events, changes in its expectations or other circumstances that exist after the date as of which the forward-looking statements were made.

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