



**The Journal of Addiction Medicine Publishes Patient-centered Outcomes from the Phase 3 Study of SUBLOCADE™ (Buprenorphine Extended-Release) Injection in Patients with Moderate to Severe Opioid Use Disorder (OUD)**

*Six monthly injections of SUBLOCADE™ improved patient health status and health-related quality of life compared to placebo in 24-week pivotal trial*

**Slough, UK and Richmond, VA, 7 March 2019** – Indivior PLC (LON: INDV) today announced the publication of patient-centered outcome endpoints (health status, physical and mental health, medication satisfaction, employment, health insurance status and healthcare resource utilization) in opioid use disorder (OUD) by the *Journal of Addiction Medicine*. These measures were collected during the 24-week, Phase 3, randomized, placebo-controlled study assessing the efficacy, safety and tolerability of SUBLOCADE™ (buprenorphine extended-release) injection for subcutaneous use (CIII)<sup>1</sup>.

*“The ultimate goal of opioid dependence treatment is to support the patient on a path towards recovery, a process leading to a healthier way of life,”* said Walter Ling, M.D., Professor Emeritus of Psychiatry and Founding Director of the Integrated Substance Abuse Programs (ISAP), University of California, Los Angeles. *“Understanding patient-centered outcomes in patients receiving treatment for OUD can help clinicians better assess the comprehensive effect of treatment and the impact of interventions on patients’ life activities and recovery journey.”*

The manuscript published [online ahead of print](#) on March 7, 2019 in *The Journal of Addiction Medicine*, is titled “Patient-centered Outcomes in Participants of a Buprenorphine Monthly Depot (BUP-XR) Double-blind, Placebo-controlled, Multicenter, Phase 3 Study.” This Phase 3 study served as one of the key studies from the clinical development program that supported the U.S. Food and Drug Administration (FDA) approval of SUBLOCADE in November 2017<sup>1</sup>. In August 2018, the FDA released a draft guidance document supporting the inclusion of patient-reported outcomes in people receiving medication-assisted treatment (MAT) for OUD<sup>2</sup>.

*“Our results show, for the first time, that compared with placebo, six monthly injections of SUBLOCADE™ improved health status and health-related quality of life. Increased medication satisfaction, increased employment, and decreased healthcare utilization were also observed.”* said Dr. Christian Heidbreder, Chief Scientific Officer, Indivior, Inc. *“We believe that these improvements will contribute to facilitate access, adherence, and retention to treatment, which will further encourage patients to continue along their pathway towards recovery.”*

In the Phase 3 trial, a total of 504 treatment-seeking adults with moderate or severe OUD were randomised to monthly SUBLOCADE 300/300 mg (6×300 mg injections), SUBLOCADE 300/100 mg (2×300 mg injections + 4×100 mg injections) or placebo (6× placebo injections) for 24 weeks and received weekly individual drug counselling<sup>1</sup>. No supplemental buprenorphine was allowed<sup>1</sup>. Measures included the EQ-5D-5L, SF-36v2<sup>®</sup>, Medication Satisfaction Questionnaire, employment/insurance status, and healthcare resource utilization (HCRU)<sup>3</sup>. Changes from baseline to the end of study were compared across treatment arms, using mixed models for repeated measures<sup>3</sup>.

The results showed that participants receiving SUBLOCADE versus placebo experienced significant changes from baseline on the EQ-5D-5L index (300/300mg: difference=0.0636,  $P=0.003$ ) and visual analog scale (300/300mg: difference=5.9,  $P=0.017$ ; 300/100mg: difference=7.7,  $P=0.002$ ), and on the SF-36v2 physical component summary score (300/300mg: difference=3.8,  $P<0.001$ ; 300/100mg: difference=3.2,  $P=0.002$ )<sup>3</sup>. Treatment satisfaction was significantly higher at the end of study for participants receiving SUBLOCADE 300/300mg (88%,  $P<0.001$ ) and 300/100mg (88%,  $P<0.001$ ) than placebo (46%)<sup>3</sup>. Employment increased by 10.8% with SUBLOCADE 300/300mg and 10.0% with 300/100mg but decreased by 12.6% with placebo<sup>3</sup>. Participants receiving SUBLOCADE compared with placebo had significantly fewer hospital days per person-year observed<sup>3</sup>.

Complete study details and results can be found in the online publication of [Journal of Addiction Medicine](#). A presentation of these results will also be made at the Academy of Managed Care Pharmacy Annual meeting on March 27, 2019 in San Diego, CA.

### **About SUBLOCADE™**

SUBLOCADE is approved by the U.S. Food and Drug Administration (FDA) for the treatment of moderate to severe OUD in adult patients who have initiated treatment with a transmucosal buprenorphine-containing product, followed by dose adjustment for a minimum of seven days<sup>4</sup>. It should be administered only by healthcare providers and should be used as part of a complete treatment program that includes counseling and psychosocial support<sup>4</sup>. The overall safety profile for SUBLOCADE, given by a healthcare provider in clinical trials, was consistent with the known safety profile of transmucosal buprenorphine, except for injection site reactions<sup>4</sup>. Adverse reactions commonly associated with SUBLOCADE (in  $\geq 5\%$  of subjects) were constipation, headache, nausea, injection site pruritus, vomiting, increased hepatic enzymes, fatigue, and injection site pain. Injection site reactions were reported in 16.5 percent of patients in Phase 3 studies<sup>4</sup>. Most of the injection site adverse reactions (ADRs) were of mild to moderate severity<sup>4</sup>. None of the injection site reactions were serious and one led to study treatment discontinuation<sup>4</sup>.

SUBLOCADE has a BOXED WARNING and is available through restricted distribution under the SUBLOCADE Risk Evaluation and Mitigation Strategy (REMS) Program<sup>4</sup>. Pursuant to the SUBLOCADE REMS, all healthcare settings and pharmacies that order and dispense SUBLOCADE must be certified and establish processes and procedures to verify the medication is dispensed directly to a healthcare provider for administration by a healthcare provider and is not dispensed directly to the patient<sup>4</sup>. Moreover, certified healthcare settings and pharmacies must not distribute, transfer, loan or sell SUBLOCADE<sup>4</sup>.

### **INDICATION AND USAGE**

SUBLOCADE is indicated for the treatment of moderate to severe opioid use disorder in patients who have initiated treatment with a transmucosal buprenorphine-containing product, followed by a dose adjustment period for a minimum of seven days.

SUBLOCADE should be used as part of a complete treatment program that includes counseling and psychosocial support.

### **IMPORTANT SAFETY INFORMATION**

**WARNING: RISK OF SERIOUS HARM OR DEATH WITH INTRAVENOUS ADMINISTRATION;  
SUBLOCADE RISK EVALUATION AND MITIGATION STRATEGY**

- **Serious harm or death could result if administered intravenously. SUBLOCADE forms a solid mass upon contact with bodily fluids and may cause occlusion, local tissue damage, and thrombo-embolic events, including life threatening pulmonary emboli, if administered intravenously.**
- **Because of the risk of serious harm or death that could result from intravenous self-administration, SUBLOCADE is only available through a restricted program called the SUBLOCADE REMS Program. Healthcare settings and pharmacies that order and dispense SUBLOCADE must be certified in this program and comply with the REMS requirements.**

Prescription use of this product is limited under the Drug Addiction Treatment Act.

**CONTRAINDICATIONS**

SUBLOCADE should not be administered to patients who have been shown to be hypersensitive to buprenorphine or any component of the ATRIGEL® delivery system.

**WARNINGS AND PRECAUTIONS**

Addiction, Abuse, and Misuse: SUBLOCADE contains buprenorphine, a Schedule III controlled substance that can be abused in a manner similar to other opioids. Monitor patients for conditions indicative of diversion or progression of opioid dependence and addictive behaviors.

Respiratory Depression: Life threatening respiratory depression and death have occurred in association with buprenorphine. Warn patients of the potential danger of self-administration of benzodiazepines or other CNS depressants while under treatment with SUBLOCADE.

Neonatal Opioid Withdrawal Syndrome: Neonatal opioid withdrawal syndrome is an expected and treatable outcome of prolonged use of opioids during pregnancy.

Adrenal Insufficiency: If diagnosed, treat with physiologic replacement of corticosteroids, and wean patient off of the opioid.

Risk of Opioid Withdrawal With Abrupt Discontinuation: If treatment with SUBLOCADE is discontinued, monitor patients for several months for withdrawal and treat appropriately.

Risk of Hepatitis, Hepatic Events: Monitor liver function tests prior to and during treatment.

Risk of Withdrawal in Patients Dependent on Full Agonist Opioids: Verify that patient is clinically stable on transmucosal buprenorphine before injecting SUBLOCADE.

Treatment of Emergent Acute Pain: Treat pain with a non-opioid analgesic whenever possible. If opioid therapy is required, monitor patients closely because higher doses may be required for analgesic effect.

**ADVERSE REACTIONS**

Adverse reactions commonly associated with SUBLOCADE (in ≥5% of subjects) were constipation, headache, nausea, injection site pruritus, vomiting, increased hepatic enzymes, fatigue, and injection site pain.

For further product information, see full [Prescribing Information](#) including BOXED WARNING and [Medication Guide](#) at [www.SUBLOCADE.com](http://www.SUBLOCADE.com).

### **About Opioid Use Disorder (OUD)**

Opioid use disorder (OUD), sometimes referred to as opioid addiction, is a chronic disease<sup>4</sup>. According to DSM-5, “OUD is characterized by signs and symptoms that reflect compulsive, prolonged self-administration of opioid substances that are used for no legitimate medical purpose or, if another medical condition is present that requires opioid treatment, they are used in doses greatly in excess of the amount needed for that medical condition<sup>5</sup>.”

Based on 2016 data from the National Survey on Drug Use and Health report, approximately 11.8 million Americans (age 12+ years) engaged in misuse of opioids in the past year<sup>6</sup>. From 1999 to 2016, the rate of deadly prescription opioid overdoses increased five-fold<sup>7</sup>. In 2016, an average of 115 people died of opioid overdose each day in the United States<sup>8</sup>. In addition, in 2016, 948,000 Americans (age 12+ years) used heroin and approximately 626,000 Americans (age 12+ years) had a heroin use disorder<sup>6</sup>. In 2016, opioids accounted for more than 70 percent of the disease burden associated with drug use disorders worldwide<sup>9</sup>.

### **About Indivior**

Indivior is a global specialty pharmaceutical company with a 20-year legacy of leadership in patient advocacy and health policy while providing education on evidence-based treatment models that have revolutionized modern addiction treatment. Our vision is for all patients around the world to have access to evidence-based treatment for the chronic conditions and co-occurring disorders of addiction. The name is the fusion of the words individual and endeavor, and the tagline “Focus on you” makes the Company’s commitment clear. Indivior is dedicated to transforming addiction from a global human crisis to a recognized and treated chronic disease. Building on its global portfolio of opioid dependence treatments, Indivior has a strong pipeline of product candidates designed to both expand on its heritage in this category and address other chronic conditions and co-occurring disorders of addiction, including alcohol use disorder and schizophrenia. Headquartered in the United States in Richmond, VA, Indivior employs more than 900 individuals globally and its portfolio of products is available in over 40 countries worldwide. Visit [www.indivior.com](http://www.indivior.com) to learn more.

### **Forward-Looking Statements**

This press release contains certain statements that are forward-looking and which should be considered, amongst other statutory provisions, in light of the safe harbor provisions of the United States Private Securities Litigation Reform Act of 1995. By their nature, forward-looking statements involve risk and uncertainty as they relate to events or circumstances that may or may not occur in the future. Actual results may differ materially from those expressed or implied in such statements because they relate to future events. Forward-looking statements include, among other things, statements regarding the Indivior Group’s financial guidance for 2018 and its medium- and long-term growth outlook, its operational goals, its product development pipeline and statements regarding ongoing litigation.

Various factors may cause differences between Indivior's expectations and actual results, including: factors affecting sales of Indivior Group’s products; the outcome of research and development activities;

decisions by regulatory authorities regarding the Indivior Group's drug applications; the speed with which regulatory authorizations, pricing approvals and product launches may be achieved; the outcome of post-approval clinical trials; competitive developments; difficulties or delays in manufacturing; the impact of existing and future legislation and regulatory provisions on product exclusivity; trends toward managed care and healthcare cost containment; legislation or regulatory action affecting pharmaceutical product pricing, reimbursement or access; claims and concerns that may arise regarding the safety or efficacy of the Indivior Group's products and product candidates; risks related to legal proceedings, including the ongoing investigative and antitrust litigation matters; the Indivior Group's ability to protect its patents and other intellectual property; the outcome of patent infringement litigation relating to Indivior Group's products, including the ongoing ANDA lawsuits; changes in governmental laws and regulations; issues related to the outsourcing of certain operational and staff functions to third parties; uncertainties related to general economic, political, business, industry, regulatory and market conditions; and the impact of acquisitions, divestitures, restructurings, internal reorganizations, product recalls and withdrawals and other unusual items.

This press release does not constitute an offer to sell or the solicitation of an offer to subscribe for or otherwise acquire or dispose of shares in the Company to any person in any jurisdiction to whom it is unlawful to make such offer or solicitation.

## **References**

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