



## **Indivior Announces New Study Data in Patients with Moderate to Severe Opioid Use Disorder (OUD) at the 50<sup>th</sup> ASAM Annual Conference**

*Injecting opioid users may benefit from higher maintenance dose of SUBLOCADE™ (buprenorphine extended-release), a once-monthly injection for the treatment of moderate to severe opioid use disorder*

*Indivior also reports results of study showing that therapeutic concentrations of buprenorphine reduce the magnitude of respiratory depression caused by fentanyl*

**Slough, UK and Richmond, VA, 6 April 2019**— Indivior PLC (LON: INDV) on Saturday announced data from two new studies: the first provides insights into dosing of once-monthly SUBLOCADE™ (buprenorphine extended-release) injection for subcutaneous use (CIII), for the treatment of moderate to severe opioid use disorder in patients who inject opioids, and the second study reports on the impact of therapeutic plasma concentrations of buprenorphine in inhibiting the respiratory depression caused by fentanyl. The results were reported at the 50<sup>th</sup> Annual Conference of the American Society of Addiction Medicine (ASAM) in Orlando, Florida and follow Friday's announcement of results from the RECOVER™ study and the 18-month long-term safety study.

“We are generating data to help the healthcare community and others understand the unique challenges faced by patients with opioid use disorder and potential ways to overcome them,” said Christian Heidbreder, Ph.D., Chief Scientific Officer of Indivior. “Addressing this crisis, one patient at a time, means having the necessary information to make individualized decisions about optimal use of medically-assisted treatment to support each patient’s recovery—including proper dosing and length of treatment.”

### *Opioid injection users may benefit from higher SUBLOCADE maintenance doses*

This post-hoc analysis investigated patterns of abstinence in both injecting and non-injecting opioid users who participated in the SUBLOCADE Phase 3 double-blind, placebo controlled pivotal trial and the subsequent SUBLOCADE open-label long-term safety study (12 months of treatment). Abstinence was defined as negative urine samples plus negative self-reports of illicit opioid use.

Injecting opioid users (based on self-reports) treated with the SUBLOCADE maintenance dose regimen of 300 mg remained in treatment longer and had a higher study completion rate than those treated with the 100 mg maintenance dose. Furthermore, the mean percentage abstinence (Weeks 10–25) was higher among injecting users treated and maintained with SUBLOCADE 300 mg (58%) vs. those maintained with SUBLOCADE 100 mg (43%); the difference in group means was 15%. Among non-injecting users, the percentage with continuous abstinence was the same (28%) in both dose groups.

These findings are consistent with previous reports that injecting opioid drug users may benefit from higher doses of methadone or buprenorphine.<sup>1,2</sup> “Indivior is planning additional studies to further characterize the patients for whom a higher maintenance dose of SUBLOCADE may be warranted,” said Dr. Heidbreder.

Participants in this post-hoc analysis were men and women age 18 to 65 years with moderate or severe opioid use disorder enrolled in a Phase 3 double-blind study and/or a Phase 3 open-label study of

SUBLOCADE. They received up to 12 once-monthly doses of SUBLOCADE and individual drug counseling in the double-blind and open-label studies. In the double-blind trial, subjects were randomized to either six SUBLOCADE 300 mg doses or two SUBLOCADE 300 mg doses followed by four 100 mg doses. Patients received either 100 mg or 300 mg dosing in the open label trial based on the medical judgment of the investigator.

*Therapeutic buprenorphine plasma concentrations reduce IV fentanyl-induced respiratory depression*

This study of eight opioid-tolerant patients showed that buprenorphine plasma concentrations of 2 ng/mL and higher that were achieved following intravenous infusion reduced the extent of respiratory depression from fentanyl. Because of its high potency, fentanyl is often added to or disguised as heroin, leading to respiratory depression and overdose deaths in users who do not know they're taking it.<sup>3</sup> Among the 70,200 U.S. drug overdose deaths estimated in 2017, the last year for which we have data, the sharpest increase was due to fentanyl.<sup>4</sup>

“Based on this study, the potential protective effect of 2 ng/ml and higher buprenorphine plasma concentrations against fentanyl-induced respiratory depression warrants additional investigation,” said Christian Heidbreder, Ph.D., Chief Scientific Officer of Indivior, Inc. The buprenorphine plasma concentrations targeted in this study were consistent with concentrations previously shown to block the drug-liking effects of illicit opioids and to significantly reduce illicit opioid use compared with placebo.<sup>5,6</sup>

The eight subjects in this study included five women and three men between the ages of 18 and 55 years who were taking either prescription or illicit opioids at daily doses of 90 mg or more oral morphine equivalents. Only two of the opioid tolerant subjects in this study were users of illicit opioids; the remaining six subjects were using prescribed opioids through a pain specialist and had no history of IV abuse. Five subjects also reported marijuana and/or cocaine use.

**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>7</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>7</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>7</sup> 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. Injection site reactions were reported in 16.5 percent of patients in Phase 3 studies.<sup>7</sup> Most of the injection site adverse reactions (ADRs) were of mild to moderate severity.<sup>7</sup> None of the injection site reactions were serious and one led to study treatment discontinuation.<sup>7</sup>

SUBLOCADE has a BOXED WARNING and is available through restricted distribution under the SUBLOCADE Risk Evaluation and Mitigation Strategy (REMS) Program.<sup>7</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>7</sup> Moreover, certified healthcare settings and pharmacies must not distribute, transfer, loan or sell SUBLOCADE.<sup>7</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>7</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>8</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>9</sup> From 1999 to 2016, the rate of deadly prescription opioid overdoses increased five-fold.<sup>10</sup> In 2017, an average of 130 people died of opioid overdose each day in the United States.<sup>11</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>9</sup> In 2016, opioids accounted for more than 70 percent of the disease burden associated with drug use disorders worldwide.<sup>12</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. Connect with Indivior on LinkedIn by visiting [www.linkedin.com/company/indivior](http://www.linkedin.com/company/indivior).

### **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 2019 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.

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