



**Indivior's RECOVER™ Study Finds Three-quarters of Patients with Moderate to Severe Opioid Use Disorder Who Received 12 monthly Injections of SUBLOCADE™ (Buprenorphine Extended-Release) Injection were Abstinent from Illicit Opioids One Year Later**



*Additional data presented at 50th ASAM Annual Conference supports 18-month safety of SUBLOCADE*

**Slough, UK and Richmond, VA, 5 April 2019**– Indivior PLC (LON: INDV) today announced data from two studies evaluating efficacy and long-term safety of once-monthly SUBLOCADE™ (buprenorphine extended-release) injection for subcutaneous use (CIII) for the treatment of moderate to severe opioid use disorder.

- The RECOVER™ study found that 75 percent of patients who had received 12 once-monthly doses of SUBLOCADE in a Phase 3 clinical trial were abstinent from illicit opioids for a year after the study ended. In this observational study, abstinence was defined as self-report confirmed by urine drug screen. Some patients had the option to continue SUBLOCADE following the clinical trial or chose to continue another form of medication-assisted treatment during the RECOVER study period.
- An 18-month safety study among SUBLOCADE-treated patients reported no new safety issues.

The results were reported at the 50<sup>th</sup> Annual Conference of the American Society of Addiction Medicine (ASAM) in Orlando, Florida.

“RECOVER is assessing real-world outcomes in patients for up to two years after they completed our clinical Phase 3 SUBLOCADE study,” said Christian Heidbreder, Ph.D., Chief Scientific Officer of Indivior, Inc. “We have invested in this research to help answer questions about how medication-assisted treatment (MAT) can help patients with opioid use disorder maintain recovery in their communities and live healthier lives.”

In addition to the long-term abstinence data being presented today, RECOVER is designed to assess patient-centered outcomes such as the impact of SUBLOCADE treatment on employment, crime, healthcare costs, family relationships and integration into society. Those findings will be reported after the conclusion of the study in December 2019.

Indivior will present findings from two additional studies on Saturday that provide insights into the impact of therapeutic plasma concentrations of buprenorphine in inhibiting the respiratory depression associated with fentanyl use, and into the response to SUBLOCADE in patients who inject illicit opioids.

*RECOVER study results: Duration of SUBLOCADE use associated with continuous abstinence from illicit opioids*

The RECOVER (Remission from Chronic Opioid Use—Studying Environmental and SocioEconomic Factors on Recovery) study found that treatment duration is a predictor of continuous abstinence from illicit opioids. Adjusted continuous abstinence rates for the year after the initial study ended ranged from a high of 75.3% for patients who had received 12 monthly SUBLOCADE study doses to a low of 24.1% for patients who had received two or fewer study doses.

“We were very pleased to see such a large proportion of patients—about three out of four—still abstinent from illicit opioids a full year after receiving 12 monthly doses of SUBLOCADE in the Phase 3 trial,” said lead author Walter Ling, M.D., Professor Emeritus of Psychiatry and Founding Director of the Integrated Substance Abuse Programs (ISAP) at UCLA. “These findings help us better understand how buprenorphine extended-release monthly injection can support a patient’s ongoing recovery.”

RECOVER enrolled 533 of 844 subjects who participated in the Phase 3 SUBLOCADE clinical trial. Eighty percent of the enrolled subjects (425 of 533) completed the one-year RECOVER survey and more than 75% completed surveys and had urine drug screens to confirm abstinence at each earlier timepoint (baseline and 3, 6 and 9 months).

Patients made independent decisions about continuing medication-assisted treatment (MAT). More than four in 10 patients (44%) were not on any MAT during the 12-month RECOVER period reported here, while 34% continued on SUBLOCADE for six or fewer months through a safety extension study, and 22% receive another form of MAT through their personal healthcare provider for some portion of the 12-month period.

*18-month long-term safety study results: No new safety issues identified with SUBLOCADE*

No new safety issues were identified among 166 patients treated with SUBLOCADE for up to 18 months in the Phase 3 clinical trial program. Except for expected injection-site reactions, which were mild to moderate in severity, the overall safety profile of SUBLOCADE was consistent with that of transmucosal buprenorphine, and the frequency and severity of treatment-emergent adverse events (TEAEs) decreased over time.

A retrospective analysis of the 18-month data also supports the efficacy of SUBLOCADE and its impact on retaining patients with opioid use disorder in treatment. The rates of abstinence from illicit opioids for patients treated with SUBLOCADE, which was defined by urine drug screen in this population of subjects, increased throughout the study from 36% to 53% at week one to 82% to 93% at 18 months. Patients who received either six or 12 once-monthly doses of SUBLOCADE also had a high probability (at least 73%) of remaining in treatment for another six months.

“These 18-month study results support the use of SUBLOCADE as an effective and well tolerated treatment for patients with opioid use disorder,” said Anne Andorn, Chief Medical Officer of Indivior, Inc. “It can be very difficult for patients to stop using illicit opioids; they and their healthcare providers should have access to a range of evidence-based treatment options, including long-acting injectables, to help patients continue to stay away from the use of illicit opioids.”

The 18-month data include treatment-seeking adults with moderate to severe opioid use disorder who received up to 18 monthly SUBLOCADE injections plus individual drug counseling as part of Indivior’s

Phase 3 clinical trial program. The Phase 3 program comprised a 24-week double-blind, placebo-controlled study, followed by an open-label 24- to 48-week safety study and then an open-label extension study.

*Indivior will present two additional studies on Saturday, April 6 at 10:00 am ET*

Results will be available on Saturday after the 8:30 am embargo. The studies examined the following:

- **Poster #100: “High Therapeutic Buprenorphine Levels Reduce IV Fentanyl Respiratory Depression”**  
This study of eight opioid-tolerant subjects examined the effect of buprenorphine plasma concentrations of 2 ng/mL and higher, infused via intravenous administration, on reducing the magnitude 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>1</sup> Previous studies have shown that buprenorphine concentrations of at least 2 ng/mL may be relevant in addressing some symptoms of OUD.<sup>2,3,4,5,6,7</sup>
- **Poster #99: “Abstinence Response to 300 mg vs 100 mg RBP-6000 among Opioid Injection Users”**  
A post-hoc analysis of data from the pivotal 24-week, Phase 3 SUBLOCADE trial evaluated abstinence among adults with a history of opioid injection versus non-injecting opioid users. Previous reports showed that injecting users may benefit from higher doses of methadone or buprenorphine.<sup>8,9</sup>

### **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>10</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>10</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>10</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>10</sup> Most of the injection site adverse reactions (ADRs) were of mild to moderate severity.<sup>10</sup> None of the injection site reactions were serious, and one led to study treatment discontinuation.<sup>10</sup>

SUBLOCADE has a BOXED WARNING and is available through restricted distribution under the SUBLOCADE Risk Evaluation and Mitigation Strategy (REMS) Program.<sup>10</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>10</sup> Moreover, certified healthcare settings and pharmacies must not distribute, transfer, loan or sell SUBLOCADE.<sup>10</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>10</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>11</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>12</sup> From 1999 to 2016, the rate of deadly prescription opioid overdoses increased five-fold.<sup>13</sup> In 2017, an average of 130 people died of opioid overdose each day in the United States.<sup>14</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>12</sup> In 2016, opioids accounted for more than 70 percent of the disease burden associated with drug use disorders worldwide.<sup>15</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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