



## **New Data from the RECOVER™ Study Reports on Abstinence, Drug Craving and Psychosocial Outcomes in People with Opioid Use Disorder following Transition from a Clinical Trial to the Real-World Setting**



*The ongoing RECOVER™ study is assessing real-world, patient-centered outcomes including abstinence from opioids and life changes, such as improved health, employment status and connection to community following treatment with SUBLOCADE™*

**Slough, UK and Richmond, VA, 17 June 2019** – Indivior PLC (LON: INDV) today announced new data from a one-year analysis of the observational RECOVER™ (Remission from Chronic Opioid Use-Studying Environmental and Socio-Economic Factors on Recovery) study examining long-term recovery in individuals with opioid use disorder after transition from a pivotal Phase III clinical trial to a real-world setting.

- Among the 212 total participants in this one-year analysis of the RECOVER study, 133 (63%) continued some form of medication for opioid use disorder (MOUD) and 79 (37%) received no further MOUD after they completed participation in a phase III clinical trial of SUBLOCADE™ (buprenorphine extended-release) injection for subcutaneous use (CIII) for the treatment of moderate to severe to severe OUD.
- Of the 79 participants who did not continue MOUD, 45 (57%) were abstinent from opioids during the first 12-month RECOVER period, while 84 of the 133 participants (63.2%) who continued MOUD were abstinent. All participants had received 12-monthly doses of SUBLOCADE during phase III trials.

The results were reported at the 81<sup>st</sup> Annual Scientific Meeting of the College on Problems of Drug Dependence (CPDD) in San Antonio, TX.

“These findings help us better understand the role of long-acting treatments, such as SUBLOCADE, in helping patients maintain long-term recovery from opioid use disorder,” said Walter Ling, M.D., Professor Emeritus of Psychiatry and Founding Director of the Integrated Substance Abuse Programs (ISAP) at UCLA, who reported the RECOVER study findings. “I am particularly excited about the data we are seeing from RECOVER because it is giving us new insights into how these patients with opioid use disorder are managing in the real world after clinical trial participation.”



RECOVER is measuring abstinence in three ways: negative urine drug screens, no self-reported past week use and a combination of both (i.e., having both a negative urine drug screen and no self-reported opioid use), which is the measure reported here.

The RECOVER study is also tracking patient success beyond measuring opioid abstinence. Participants who did not continue MOUD experienced less drug craving than participants who continued MOUD, which investigators suggest may indicate less pre-occupation with drug memories and successful avoidance of drug triggers in the no MOUD group. Participants in both groups reported similar rates of psychological distress and depression, as well as functional impairment like the inability to meet daily family, work or school responsibilities, which are common challenges for patients recovering from opioid use disorder.

### **About the RECOVER™ Study**

The RECOVER (Remission from Chronic Opioid Use-Studying Environmental and Socio-Economic Factors on Recovery) study is a multisite, non-interventional cohort study examining long-term recovery in individuals with moderate to severe opioid use disorder who received at least one dose of study treatment during the Phase III clinical trials (NCT02357901 and NCT02510014) for SUBLOCADE.<sup>1</sup> Results are being analyzed to understand the clinical, socio-economic and environmental factors associated with continuous effects of MOUD after a clinical trial.<sup>1</sup>

Participants (n=533) were eligible to join the RECOVER study 28 days after completing or terminating participation in the SUBLOCADE Phase III trials.<sup>1</sup> The RECOVER study uses data from three main sources: self-administered assessments from enrolled individuals, urine drug screens (UDS) and data collected from several public sources.<sup>1</sup> Recovery is examined over 24 months – the self-administered assessment and UDS results are completed by participants every three months over the course of this period.<sup>1</sup>

“Our investment in the RECOVER study reflects our commitment to tracking patient progress in the short-, medium- and long-term to continue to empower patients and providers with information that helps them treat their opioid use disorder,” said Christian Heidbreder, Ph.D., Chief Scientific Officer of Indivior.

### **Post-hoc analysis evaluates abstinence responses to monthly SUBLOCADE maintenance doses of 300 mg versus 100 mg in people who inject opioids**

Indivior presented new post-hoc analyses from SUBLOCADE 24-week Phase III clinical trials suggesting that people with moderate to severe opioid use disorder who inject opioids may benefit from the higher 300 mg once-monthly SUBLOCADE maintenance dose. SUBLOCADE is administered as two initial monthly doses of 300 mg followed by monthly maintenance doses of either 100 mg (300/100 mg) or 300 mg (300/300 mg).

Non-injecting opioid users achieved maximal response at buprenorphine plasma concentrations of 2.5 to 3 ng/mL, while injecting opioid users achieved maximal response at concentrations closer to 6 ng/mL. These laboratory findings aligned with improved clinical outcomes showing a significantly higher mean percentage of abstinence among injecting users maintained on the 300 mg dose (60.1%) compared to those maintained on the 100 mg dose (45.3%) for a risk-adjusted difference of just under 15%.



“The SUBLOCADE dosing regimens were designed to deliver sustained buprenorphine plasma concentrations of at least 2 ng/mL that are needed to block the subjective effects of opioids in most subjects,” according to Dr. Heidbreder, “But years of experience working to improve outcomes for patients with opioid use disorder have taught us that treatment options are not one-size-fits-all. Indivior is planning additional studies to further characterize the patients who may benefit from the higher maintenance dose of SUBLOCADE.”

### **About SUBLOCADE™**

SUBLOCADE is approved by the U.S. Food and Drug Administration (FDA) for the treatment of moderate to severe opioid use disorder in adult patients who have initiated treatment with a transmucosal buprenorphine-containing product, followed by dose adjustment for a minimum of seven days.<sup>2</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>2</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>2</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% of patients in Phase 3 studies.<sup>2</sup> Most of the injection site adverse reactions (ADRs) were of mild to moderate severity.<sup>2</sup> None of the injection site reactions were serious, and one led to study treatment discontinuation.<sup>2</sup>

SUBLOCADE has a BOXED WARNING and is available through restricted distribution under the SUBLOCADE Risk Evaluation and Mitigation Strategy (REMS) Program.<sup>2</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>2</sup> Moreover, certified healthcare settings and pharmacies must not distribute, transfer, loan or sell SUBLOCADE.<sup>2</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**

Addition, 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  $\geq 5\%$  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>2</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>3</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>4</sup> From 1999 to 2017, the rate of deadly prescription opioid overdoses increased five-fold.<sup>5</sup> In 2017, an average of 130 people died of opioid overdose each day in the United States.<sup>6</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>4</sup> In 2016, opioids accounted for more than 70% of the disease burden associated with drug use disorders worldwide.<sup>7</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 800 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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