



New Analysis From One-Year Study of Monthly Buprenorphine Extended-Release Injections Showed Improved or Stable Patient-Centered Outcomes

— Sustained improvements in multiple health outcomes following twelve monthly buprenorphine extended-release injections in patients with opioid use disorder —

— Findings published in the Journal of Substance Abuse Treatment —

Slough, UK and Richmond, VA, December 2, 2019 – Indivior PLC (LON: INDV) announced today that new analysis from a 12-month investigation of monthly buprenorphine extended-release injections showed that study participants who were treated with SUBLOCADE® (buprenorphine extended-release) injection, for subcutaneous use (CIII), demonstrated improved or maintained patient-centered outcomes across the following measures:

- Health status and health-related quality of life,
- Employment/insurance status,
- Healthcare resource utilization,
- Medication satisfaction,
- Treatment effectiveness and improvement in addiction severity as measured by a patient reported Addiction Severity Index.¹

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.²

“This analysis offers new insight into extended-release buprenorphine treatment in patients with opioid use disorder on important measures of patient-centered outcomes that extend beyond abstinence and treatment retention,” said the study’s lead author, Walter Ling, MD, Research Professor, Department of Family Medicine, David Geffen School of Medicine, UCLA. “These results showed that patients experienced improvements in physical and mental health which may help in the recovery journey and positively impact lifestyle, including employment.”

The study, entitled, “*Effects of monthly buprenorphine extended-release injections on patient-centered outcomes: a long-term study*” was published online in the December issue of the Journal of Substance Abuse Treatment (<https://doi.org/10.1016/j.jsat.2019.11.004>).¹

By the end of the 12-month study, patient-reported outcomes included:

- 88% of the 206 study participants reported medication satisfaction,

- Treatment Effectiveness Assessment scores improved, and quality of life scores were stable or improved¹,
- Employment rate increased by 7% from 44.2% to 51.2 %.¹

Health insurance coverage remained stable at approximately 55%. Health care utilization during the 3,604-person-months of the study included 21 hospitalizations, 140 emergency department visits and 923 outpatient services.¹ Rates of observed hospitalizations, emergency, and outpatient service visits were much lower than utilization observed in a claims analysis focusing on participants receiving buprenorphine medication-assisted treatment.³ Confidence intervals did not cross zero for all comparisons.¹

“These 12-month findings strengthen our original observations⁶ that previously showed that participants receiving SUBLOCADE® over a 6-month period reported better health, higher medication satisfaction, increased employment, and decreased healthcare utilization compared to placebo,” said Christian Heidbreder, PhD, Indivior’s Chief Scientific Officer. “These findings also show that patient-centered outcomes that can be measured during office visits may help clinicians assess their patient’s improvement.”

Medication-assisted treatment (MAT) combines medication and counseling to treat both the physical and behavioral parts of opioid addiction, with the goal of helping people achieve and maintain recovery.^{4,5} The combination of medicine and psychosocial therapy have been proven successful in treating OUD and can help extend recovery.^{4,5} In fact, MAT has been shown to be more effective than either medication or counseling alone.⁵

About the Study¹

This study was a multi-center, open-label, long-term clinical safety study (NCT02510014) evaluating up to 12 months of buprenorphine extended-release injection therapy in people 18 to 65 years of age who were seeking treatment for moderate or severe OUD as defined in the Diagnostic Statistical Manual 5 (DSM-5) (American Psychiatric Association, 2013). The study included patients who completed the randomized, double-blind, placebo-controlled study (NCT02357901, RB-US-13-0001) and patients that did not participate in study RB-US-13-0001. This analysis focused on patients who did not participate in study RB-US-13-0001. The data reported are for patient-centered outcome measures which were a tertiary outcome of the study.

Following a 7-day screening period, these subjects received treatment with a 3- to 14-day run-in period with sublingual buprenorphine/naloxone, titrated to a maximum dose of 24 mg daily based on clinical response and physician judgement; followed by up to 12 monthly injections of SUBLOCADE.

All participants received an initial 300 mg subcutaneous injection. For subsequent doses, the SUBLOCADE dose could be reduced to 100 mg and then increased back to 300 mg, based on the medical judgment of the investigator. All participants received injections of SUBLOCADE separated by 28 (-2/+ 4) days. A 4-week follow-up period was used to assess any further safety signals after the last dose. Patient-centered outcome measures including health related quality of life measures (E5-QD-5L Index, EQ5D-5L VAS, SF-36v2), Treatment Effectiveness Assessment, Addiction Severity Index-

Lite, and Medication Satisfaction Questionnaire were performed periodically and longitudinally throughout the study.

About SUBLOCADE®

SUBLOCADE (buprenorphine extended-release) injection, for subcutaneous use (CIII) is a prescription medicine used to treat adults with moderate to severe addiction (dependence) to opioid drugs (prescription or illegal) who have received an oral transmucosal (used under the tongue or inside the cheek) buprenorphine-containing medicine at a dose that controls withdrawal symptoms for at least 7 days. SUBLOCADE is part of a complete treatment plan that should include counseling.²

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.² 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.² Most of the injection site adverse reactions (ADRs) were of mild to moderate severity.² None of the injection site reactions were serious, and one led to study treatment discontinuation.² SUBLOCADE has a BOXED WARNING and is available through restricted distribution under the SUBLOCADE Risk Evaluation and Mitigation Strategy (REMS) Program.² 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.² Moreover, certified healthcare settings and pharmacies must not distribute, transfer, loan or sell SUBLOCADE.²

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

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

**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 body 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.**

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.

About Opioid Use Disorder (OUD)

Opioid addiction isn't a moral weakness. Opioid addiction is a chronic disease called Opioid Use Disorder (OUD)⁷ in which people develop a pattern of using opioids that can lead to negative consequences.⁴ Opioid addiction may affect the parts of the brain that control impulses, judgment, and decision-making.^{4,5} Patients become trapped in a cycle of opioid use, which produces changes in brain function that can reduce their ability to control their use.^{4,8}

In 2018, an estimated 10.3 million people aged 12 or older misused opioids in the past year, including 9.9 million prescription pain reliever misusers and 808,000 heroin users. Approximately 506,000 people misused prescription pain relievers and used heroin in the past year.⁹ SUBLOCADE is not indicated for use in children younger than 18 years of age. Buprenorphine, the active ingredient of SUBLOCADE can cause severe, possibly fatal, respiratory depression in children who are accidentally exposed to it.²

About Indivior

Indivior is a global pharmaceutical company working to help change patients' lives by developing medicines to treat addiction and serious mental illnesses. Our vision is that all patients around the world will have access to evidence-based treatment for the chronic conditions and co-occurring disorders of addiction. 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 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. 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 to learn more. Connect with Indivior on LinkedIn by visiting 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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References

1. Ling, W., Nadipelli, V. R., Solem, C. T., Ronquest, N. A., Yeh, Y.-C., Learned, S. M., ... Heidbreder, C. (2019). Effects of monthly buprenorphine extended-release injections on patient-centered outcomes: A long-term study. *Journal of Substance Abuse Treatment*. doi: 10.1016/j.jsat.2019.11.004.
2. SUBLOCADE® [Prescribing Information]. Indivior Inc., North Chesterfield, VA. October 2019.
3. Ronquest, N. A., Willson, T. M., Montejano, L. B., Nadipelli, V. R., & Wollschlaeger, B. A. (2018). Relationship between buprenorphine adherence and relapse, health care utilization and costs in privately and publicly insured patients with opioid use disorder. *Substance abuse and rehabilitation, 9*, 59-78. doi:10.2147/SAR.S150253
4. U.S. Department of Health and Human (HHS), Services Substance Abuse and Mental Health Services Administration Center for Substance Abuse Treatment (SAMHSA). *Medication-Assisted Treatment for Opioid Addiction*. HHS Publication No. (SMA) 09-4443, First printed 2009. Revised 2011.
5. U.S. Department of Health and Human Services (HHS), National Institute on Drug Abuse, National Institutes of Health. *Drugs, Brains, and Behavior: The Science of Addiction*. HHS Publication No. (SMA) 18-5063PT5, Printed 2018.
6. Ling W, Nadipelli VR, Solem CT, Ronquest NA, Yeh Y-C, Learned SM, Mehra V, Heidbreder C (2019) Life-activity Outcomes in Participants of a Buprenorphine Monthly Depot (BUP-XR) Double-blind, Placebo-controlled, Multicenter, Phase 3 Study. *J Addiction Med*, 13(6): 442-449. <https://doi.org/10.1097/ADM.0000000000000517>

7. U.S. Department of Health and Human Services (HHS), Office of the Surgeon General. *Facing Addiction in America: The Surgeon General's Report on Alcohol, Drugs, and Health*. Washington, DC: HHS, November 2016.

8. Volkow ND, Koob GF, McLellan AT. Neurobiologic advances from the brain disease model of addiction. *N Engl J Med*. 2016; 374:363-371.

9. Substance Abuse and Mental Health Services Administration. *Key substance use and mental health indicators in the United States: Results from the 2018 National Survey on Drug Use and Health*. HHS Publication No. PEP19-5068, NSDUH Series H-54. Rockville, MD: Center for Behavioural Health Statistics and Quality, Substance Abuse and Mental Health Services Administration. Retrieved from <https://www.samhsa.gov/data/>. Accessed on November 7, 2019.

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