FDA Approves SUBLOCADE™ (Buprenorphine Extended-Release), the First and Only Once-Monthly Injectable Buprenorphine Formulation to Treat Moderate to Severe Opioid Use Disorder

SUBLOCADE Expected to be Available to U.S. Patients in Q1 2018

This announcement contains inside information.

Slough, UK and Richmond, VA, 30 November 2017 – Indivior PLC (LON: INDV) today announced that the U.S. Food and Drug Administration (FDA) has approved SUBLOCADE™ *(buprenorphine extended-release) injection for subcutaneous use (CIII)*, the first and only once-monthly injectable buprenorphine formulation for the treatment of moderate to severe opioid use disorder (OUD) in patients who have initiated treatment with a transmucosal buprenorphine-containing product followed by dose adjustment for a minimum of seven days. SUBLOCADE is intended to be administered only by healthcare providers and should be used as part of a complete treatment program that includes counseling and psychosocial support[1]. SUBLOCADE is expected to be available to patients in the U.S. in Q1 2018.

"SUBLOCADE is a scientific innovation that represents a new treatment option to help patients attain more illicit opioid-free weeks during their treatment program," said Shaun Thaxter, Chief Executive Officer of Indivior. "In the Opioid Blockade Study, SUBLOCADE achieved complete blockade of drug-liking effects for a full month in most patients. SUBLOCADE is the first and only therapy that, at steady state, delivers buprenorphine at a sustained rate of at least 2 ng/mL over a one month period. The urgency for this new treatment has never been greater, as the U.S. opioid crisis has been declared a national public health emergency. SUBLOCADE's approval is an important step forward for patients, families and communities battling the opioid epidemic."

SUBLOCADE contains buprenorphine, a partial agonist at the mu-opioid receptor[1]. Mu-opioid receptors in the brain are known to mediate the subjective effects of opioids, including drug-liking, which is the pleasure associated with opioid use[2]. SUBLOCADE delivers sustained plasma levels of buprenorphine that translate into high mu-opioid receptor occupancy in the brain, which blocks the drug-liking effects of opioids[1].

In the SUBLOCADE clinical trial program, average buprenorphine plasma concentrations of 2-3 ng/mL were associated with mu-opioid receptor occupancy ≥70% and the reduction of illicit opioid use. SUBLOCADE 300 mg delivers average buprenorphine plasma levels of approximately 2 ng/mL after the first injection. The average concentration of SUBLOCADE at steady-state was 3.21 ng/mL and 6.54 ng/mL for the 100 mg and 300 mg doses, respectively[1].

Indivior conducted an Opioid Blockade Study (RB-US-13-0002) which investigated the ability of SUBLOCADE 300 mg to block the subjective effects of illicit opioids, including drug-liking. In the 12-week trial evaluating the blocking effect, SUBLOCADE 300 mg fully blocked the drug-liking effects of hydromorphone[1]. Hydromorphone is a potent opioid pain medication[3] that is commonly used in human studies to evaluate opioid drug-liking[2].

SUBLOCADE was evaluated in a 24-week, Phase 3 pivotal study (RB-US-13-0001) in which patients were randomized to one of the following three regimens: six once-monthly SUBLOCADE 300 mg doses; two once-monthly SUBLOCADE 300 mg doses followed by four once-monthly 100 mg doses; or six once-monthly injections of placebo. Both dosage regimens of SUBLOCADE were shown to be superior to placebo in achieving more illicit opioid-free weeks ($p<0.0001$)[1,4]. In the clinical trials, the overall safety profile for SUBLOCADE, given by a healthcare provider, was consistent with the known safety profile of transmucosal buprenorphine, except for injection site reactions. The most common adverse reactions (≥5% patients), included constipation, nausea, vomiting, abnormal liver enzymes, headache, sedation and somnolence. Injection site reactions were reported in 16.5% of the patients. None of the injection site reactions were serious, and only one led to study treatment discontinuation[1].

“Every patient’s journey to recovery is different and they face many challenges. To help support these differences, doctors and patients need options for medication-assisted treatment,” said Dr. Brent Boyett, SUBLOCADE clinical investigator and director at Boyett Health Services, Inc. “In a Phase 3 clinical study, SUBLOCADE helped patients refrain from illicit opioids for more weeks compared to placebo. Used in combination with counseling and psychosocial support, SUBLOCADE is a transformational new drug that offers a treatment option for people with moderate to severe opioid use disorder.”

The opioid addiction epidemic in the U.S. is a national public health emergency, with nearly 12 million people impacted nationwide and an average of four people dying from opioid overdose every hour of every day[5,6,7]. OUD, commonly referred to as opioid addiction[8], is a chronic disease that changes the brain[9]. The patient journey to treatment and recovery is complex, with many barriers such as social stigma, access to treatment and prescribers, and difficulty adhering to treatment plans. Out of the more than 2.5 million patients diagnosed with OUD in the U.S., less than half are treated with medication-assisted treatment (MAT)[10].

The economic impact of the opioid epidemic to the healthcare system is significant. The amount paid for treatment of substance use disorders is only a small portion of the costs these disorders impose on society. Data published in 2016 presented the total costs of prescription opioid use disorder and overdose in the U.S. at $78 billion in 2013. Of that, only 3.6 percent, or about $2.8 billion, was for treatment[11]. A separate, recent analysis by the White House Council of Economic Advisers estimated the total annual cost of prescription opioid overdose, abuse and dependence in the U.S. at $504 billion in the year 2015[12]. Patients, physicians, policymakers and other stakeholders have expressed the need for additional treatment options in the fight against the chronic relapsing disease of opioid addiction. Indivior has an ongoing, prospective, observational study (RECOVER™) to understand the clinical, environmental and socioeconomic characteristics of OUD patients[13].

“The American Society of Addiction Medicine supports the development and manufacturing of medications that aid in the treatment of addiction,” said Dr. Kelly Clark, President, American Society

of Addiction Medicine. “The introduction of novel pharmacotherapies supports this goal. Addiction patients, like all patients, should have available to them a robust and varied array of treatment options, as no one treatment modality is appropriate or therapeutic for everyone.”

“We applaud the scientists and leaders who have been working tirelessly on the development of new, longer-acting medicines for the treatment of opioid use disorder. These exciting new developments will help our patients and families live healthy lives and accelerate the progress in the treatment of addiction,” commented Jessica Hulsey Nickel, President and CEO of the Addiction Policy Forum.

Under the Drug Addiction Treatment Act (DATA) codified at 21 U.S.C. 823(g), prescription use of SUBLOCADE in the treatment of opioid dependence is limited to healthcare providers who meet certain qualifying requirements, and who have notified the Secretary of Health and Human Services (HHS) of their intent to prescribe this product for the treatment of opioid dependence and have been assigned a unique identification number that must be included on every prescription[1].

SUBLOCADE will be distributed through a restricted distribution system, which is intended to prevent the direct distribution to a patient. This is because of risk of serious harm or death that could result from intravenous self-administration.

Indivior worked closely with the FDA to include appropriate warnings and precautions, including a BOXED WARNING in the label and implementation of a Risk Evaluation and Mitigation Strategy (REMS) program. Healthcare settings and pharmacies that order and dispense SUBLOCADE must be certified in the SUBLOCADE REMS Program. In addition, Indivior continues to enhance its compliance program to keep pace with the anticipated increase in the number of patients in treatment.

For further information, see **SUBLOCADE: Product Details, Clinical Information and Price Fact Sheet**.

About SUBLOCADE ™

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.

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.**

IMPORTANT SAFETY INFORMATION
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.

The full prescribing information, including BOXED WARNING, for SUBLOCADE can be found here: http://indivior.com/wp-content/uploads/2017/11/SUBLOCADE-Prescribing-Information.pdf.

About Opioid Use Disorder

OUD, commonly referred to as opioid addiction[8], is a chronic, relapsing disease that changes the brain[9]. According to the DSM–5, opioid use disorder 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[13].

Based on 2016 data from the most recent National Survey on Drug Use and Health report, nearly 12 million Americans (age 12+ years) engaged in misuse of opioids in the last year[6]. Between 1999 and 2014 the rate of deadly opioid overdoses quadrupled[14], and in the United States alone, an average of four people die of opioid overdose every hour of every day[7]. In 2015 opioids accounted for 70 percent of the negative health impact associated with drug use disorders worldwide[15]. Approximately 2.5 million American adults (age 18+ years old) met criteria for opioid use disorder in the past year[10]. The same report suggested that 935,000 adults have used heroin in the past year and 471,000 used in the past month. There were approximately 625,000 adults who had a heroin use disorder in the past year[6]. In a recent report by the White House Council of Economic Advisers, estimated economic costs of the opioid crisis in the U.S. were $504 billion in 2015[12].

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. The name is the fusion of the words individual and endeavour, 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 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 harbour 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 will or may 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 our financial guidance for 2017 and our medium- and long-term growth outlook, our operational goals, our 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; 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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