



## **Indivior PLC Presents Results from the Phase 3 Pivotal Study of RBP-6000 Buprenorphine Monthly Depot for the Treatment of Opioid Use Disorder**

*Data Presented in Late-Breaking Research Oral Session at CPDD 79<sup>th</sup> Annual Scientific Meeting 2017*

**Slough, UK, and Richmond, VA, 21 June 2017** – Indivior PLC (LON: INDV) today announced the presentation of results from its pivotal Phase 3 clinical trial (RB-US-13-0001) evaluating the efficacy and safety of RBP-6000, an investigational once-monthly injectable buprenorphine in the ATRIGEL® delivery system for the treatment of adults with moderate-to-severe opioid use disorder (OUD) as part of a complete treatment plan to include counseling and psychosocial support. The 24-week study met its primary and key secondary endpoints for both dosage regimens of RBP-6000, which demonstrated clinically and statistically significant differences in percentage abstinence and treatment success, defined as any subject with  $\geq 80\%$  of urine samples negative for opioids combined with self-reports negative for illicit opioid use from Weeks 5 to 24, compared to placebo. The study results were presented in a late-breaking research oral presentation at the 79<sup>th</sup> Annual Scientific Meeting of the College on Problems of Drug Dependence (CPDD) meeting in Montreal<sup>†</sup>.

“The clinical data from our Phase 3 study also showed that outcomes with RBP-6000 are consistent across other secondary clinical endpoints, including control of craving and withdrawal symptoms, as compared to placebo,” said Christian Heidbreder, Ph.D., Chief Scientific Officer of Indivior. “These outcomes started with the first dose of RBP-6000, which achieved buprenorphine plasma concentrations  $\geq 2$  ng/mL and predicted whole brain mu-opioid receptor occupancy of  $\geq 70\%$ , and were also maintained for the one-month dosing intervals and for the entire treatment duration.”

These results were confirmed by exposure-response analyses demonstrating a relationship between buprenorphine plasma concentrations, abstinence, withdrawal symptoms and opioid craving.

“Opioid use disorder is a chronic, relapsing medical condition with multiple factors playing a role and impacting patient outcomes, including control of withdrawal symptoms, cravings and relapse to illicit opioid use,” said Amit Vijapura, M.D, psychiatrist, and study principal investigator. “If approved, RBP-6000 could help address the unmet needs of patients and represent a potentially important new option for the treatment of opioid use disorder.”

In this study, RBP-6000 was generally well tolerated and had a safety profile consistent with that of transmucosal buprenorphine with no unexpected safety findings. Injection site reactions were not treatment-limiting and resulted in less than 1% of subjects discontinuing treatment. The most common (reported in  $\geq 5\%$  of subjects) treatment-emergent adverse events (TEAEs) reported in the active total group were headache, constipation, nausea, injection site pruritus, vomiting, insomnia and upper respiratory tract infection.

Last month, Indivior submitted a New Drug Application (NDA) to the U.S. Food and Drug Administration (FDA) to seek marketing approval for RBP-6000 for the treatment of adults with moderate-to-severe OUD as part of a complete treatment plan to include counseling and psychosocial support.

### **Phase 3 Pivotal Study Results and Design (RB-US-13-0001)**

The Phase 3 study evaluated the efficacy and safety of RBP-6000 over 24 weeks of treatment for moderate-to-severe OUD. A total of 504 treatment-seeking adults, aged 19 to 64 with moderate or severe OUD (not currently receiving medication-assisted treatment, or MAT) were randomized to either one of two dosage regimens of RBP-6000 (n=404) or placebo (n=100). Prior to randomization, subjects were inducted and dose-stabilized onto transmucosal buprenorphine-containing product according to the prescribing information to suppress opioid withdrawal signs and symptoms and ensure lack of allergy to buprenorphine. In this study, SUBOXONE® (buprenorphine and naloxone) sublingual film was used for induction. Subjects were considered dose-stabilized when cravings and withdrawal symptoms were clinically controlled ( $\leq 20$  on a 100 point Opioid Craving visual analog scale [VAS] and  $\leq 12$  on a 48 point clinical opiate withdrawal scale [COWS] for a minimum of 24 hours). After randomization, supplemental dosing with any buprenorphine-containing product was not permitted during the study.

Randomized subjects received 6 once-monthly 300 mg doses (300/300 mg), 2 once-monthly 300 mg doses followed by 4 once-monthly 100 mg doses (300/100 mg), or 6 once-monthly subcutaneous injections of placebo. All doses were administered in-clinic by a physician or suitably qualified designee and were separated by  $28 \pm 2$  days. In addition to study medication, all subjects received manual-guided psychosocial support at least once a week (Individual Drug Counseling).

The study's primary efficacy endpoint was the mean percentage abstinence (opioid-free weeks), assessed as a cumulative distribution function (CDF) and measured by the percentage of urine samples negative for opioids, combined with self-reports negative for illicit opioid use, from Week 5 to Week 24. The key secondary endpoint was treatment success, defined as any subject with  $\geq 80\%$  of urine samples negative for opioids combined with self-reports negative for illicit opioid use from Weeks 5 to 24. Additional secondary measures included the proportion of study completers as well as subjects' scores on both the Opioid Craving VAS and the COWS. The safety of RBP-6000 was also assessed relative to placebo.

The results showed that RBP-6000 met the primary efficacy endpoint, with both RBP-6000 dosage regimens demonstrating abstinence rates that were significantly higher versus placebo (300/300 mg: 41.3%; 300/100 mg: 42.7%; placebo: 5.0%,  $p < 0.0001$ ). Both RBP-6000 dosages also met the key secondary endpoint of treatment success (300/300 mg: 29.1%; 300/100 mg: 28.4%; placebo: 2.0%,  $p < 0.0001$ ). In addition to the efficacy findings, a pharmacokinetic-pharmacodynamic (exposure-response) analysis demonstrated a positive relationship between buprenorphine exposure, mu-opioid receptor occupancy and clinical endpoints of abstinence, withdrawal symptoms and opioid craving.

Significantly more subjects in both RBP-6000 dosage groups completed the study compared with those on placebo (300/300 mg: 64.3%; 300/100 mg: 61.3%; placebo: 33.3%,  $p < 0.0001$ ). RBP-6000 was generally well tolerated in the Phase 3 study. 2.7% of subjects on RBP-6000 (both dosage regimens combined) experienced a serious treatment-emergent adverse event (TEAE) compared with 5.0% of subjects on placebo. There were no related serious TEAEs across groups. 6.9% of subjects on RBP-6000 (both dosage regimens combined) experienced a severe TEAE compared with 4.0% of subjects on placebo. 4.2% of subjects on RBP-6000 (both dosage regimens combined) discontinued treatment due

to TEAEs compared with 2.0% of subjects on placebo. The most common (reported in  $\geq 5\%$  of subjects) TEAEs reported in the active total group were headache, constipation, nausea, injection site pruritus, vomiting, insomnia and upper respiratory tract infection. In this study, RBP-6000 had a safety profile consistent with that of transmucosal buprenorphine with no unexpected safety findings.

### **Investor Event Following the CPDD Presentation**

Indivior will host a webcast event on June 29<sup>th</sup>, 2017 for the investment community on RBP-6000, along with a question and answer session. Participation details will be made available shortly. The presentation will be posted on Indivior.com.

### **About RBP-6000**

**RBP-6000 IS AN INVESTIGATIONAL PRODUCT THAT HAS NOT BEEN APPROVED BY THE U.S. FOOD AND DRUG ADMINISTRATION FOR SAFETY AND EFFICACY.**

RBP-6000 is an investigational buprenorphine sustained-release formulation using the ATRIGEL<sup>®</sup> delivery system, which consists of a polymeric solution of a biodegradable poly-(DL-lactide-co-glycolide) co-polymer dissolved in N-methyl pyrrolidone (NMP), a water-miscible biocompatible solvent. After subcutaneous injection, NMP diffuses out of the polymer matrix and the polymer precipitates, trapping the drug inside and forming an amorphous solid depot *in situ*. The depot releases buprenorphine over a one-month period by diffusion as the polymer biodegrades.

### **About Opioid Use Disorder**

According to the DSM-5<sup>1</sup>, 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.

Based on 2015 data from the most recent National Survey on Drug Use and Health report, 11.5 million American adults (age 18+ years old) engaged in misuse of prescription pain relievers, including opioids, in the last month. Approximately 1.9 million American adults met criteria for prescription pain reliever use disorder in the past year. The same report suggested that 5.1 million adults have used heroin at some point in their lives, with 807,000 using in the past year and 324,000 using in the past month. There were approximately 585,000 adults who had a heroin use disorder in the past year<sup>2</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. 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](http://www.indivior.com) to learn more.

## **IMPORTANT SAFETY INFORMATION**

### **Indication**

SUBOXONE® (buprenorphine and naloxone) Sublingual Film (CIII) is a prescription medicine indicated for treatment of opioid dependence and should be used as part of a complete treatment plan to include counseling and psychosocial support.

**Treatment should be initiated under the direction of healthcare providers qualified under the Drug Addiction Treatment Act.**

### **Important Safety Information**

Do not take SUBOXONE Film if you are allergic to buprenorphine or naloxone as serious negative effects, including anaphylactic shock, have been reported.

SUBOXONE Film can be abused in a manner similar to other opioids, legal or illicit.

SUBOXONE Film contains buprenorphine, an opioid that can cause physical dependence with chronic use. Physical dependence is not the same as addiction. Your healthcare provider can tell you more about the difference between physical dependence and drug addiction. Do not stop taking SUBOXONE Film suddenly without talking to your healthcare provider. You could become sick with uncomfortable withdrawal symptoms because your body has become used to this medicine.

SUBOXONE Film can cause serious life-threatening breathing problems, overdose and death, particularly when taken by the intravenous (IV) route in combination with benzodiazepines or other medications that act on the nervous system (ie, sedatives, tranquilizers or alcohol). It is extremely dangerous to take nonprescribed benzodiazepines or other medications that act on the nervous system while taking SUBOXONE Film.

You should not drink alcohol while taking SUBOXONE Film, as this can lead to loss of consciousness or even death.

Death has been reported in those who are not opioid dependent.

Your healthcare provider may monitor liver function before and during treatment.

SUBOXONE Film is not recommended in patients with severe hepatic impairment and may not be appropriate for patients with moderate hepatic impairment. However, SUBOXONE Film may be used with caution for maintenance treatment in patients with moderate hepatic impairment who have initiated treatment on a buprenorphine product without naloxone.

Keep SUBOXONE Film out of the sight and reach of children. Accidental or deliberate ingestion of SUBOXONE Film by a child can cause severe breathing problems and death.

Do not take SUBOXONE Film before the effects of other opioids (eg, heroin, hydrocodone, methadone, morphine, oxycodone) have subsided as you may experience withdrawal symptoms.

Injecting the SUBOXONE Film product may cause serious withdrawal symptoms such as pain, cramps, vomiting, diarrhea, anxiety, sleep problems and cravings.

Before taking SUBOXONE Film, tell your healthcare provider if you are pregnant or plan to become pregnant. If you are pregnant, tell your healthcare provider as withdrawal signs and symptoms should be monitored closely and the dose adjusted as necessary. If you are pregnant or become pregnant while taking SUBOXONE Film, alert your healthcare provider immediately and you should report it using the contact information provided below.\*

Opioid-dependent women on buprenorphine maintenance therapy may require additional analgesia during labor.

Neonatal opioid withdrawal syndrome (NOWS) is an expected and treatable outcome of prolonged use of opioids during pregnancy, whether that use is medically-authorized or illicit. Unlike opioid withdrawal syndrome in adults, NOWS may be life-threatening if not recognized and treated in the neonate. Healthcare professionals should observe newborns for signs of NOWS and manage accordingly.

Before taking SUBOXONE Film, talk to your healthcare provider if you are breastfeeding or plan to breastfeed your baby. The active ingredients of SUBOXONE Film can pass into your breast milk. You and your healthcare provider should consider the development and health benefits of breastfeeding along with your clinical need for SUBOXONE Film and should also consider any potential adverse effects on the breastfed child from the drug or from the underlying maternal condition.

Do not drive, operate heavy machinery or perform any other dangerous activities until you know how SUBOXONE Film affects you. Buprenorphine in SUBOXONE Film can cause drowsiness and slow reaction times during dose-adjustment periods.

Common side effects of SUBOXONE Film include nausea, vomiting, drug withdrawal syndrome, headache, sweating, numb mouth, constipation, painful tongue, redness of the mouth, intoxication (feeling lightheaded or drunk), disturbance in attention, irregular heartbeat, decrease in sleep, blurred vision, back pain, fainting, dizziness and sleepiness.

This is not a complete list of potential adverse events associated with SUBOXONE Film. Please see [full Prescribing Information](#) for a complete list.

\*To report pregnancy or side effects associated with taking SUBOXONE Film, please call 1-877-782-6966. You are encouraged to report negative side effects of prescription drugs to the FDA. Visit [www.fda.gov/medwatch](http://www.fda.gov/medwatch) or call 1-800-FDA-1088.

For more information about SUBOXONE Film, SUBOXONE<sup>®</sup> (buprenorphine and naloxone) Sublingual Tablets (CIII), or SUBUTEX<sup>®</sup> (buprenorphine) Sublingual Tablets (CIII), please see the respective [full Prescribing Information](#) and [Medication Guide](#) at [www.suboxoneREMS.com](http://www.suboxoneREMS.com).

## **Forward-Looking Statements**

This presentation 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.

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<sup>†</sup> *Indivior previously shared Phase 3 study results on March 28, 2017. Please see <http://www.indivior.com/investor-news/rbp-6000-phase-3-pkpdro-heor-subanalyses/> for more information.*

#### REFERENCES

1. American Psychiatric Association (2013). Diagnostic and statistical manual of mental disorders (5th ed.). Arlington, VA: American Psychiatric Publishing.
2. "National Survey on Drug Use and Health 2015." *Substance Abuse and Mental Health Data Archive Public Surveys*. <https://pdas.samhsa.gov/#/?k=o2r5ed>. Accessed on 02 Mar. 2017.