

# Indivior R&D Update

## May 2019

## R&D / Pipeline Update

### Treatment of Opioid Use Disorder (OUD)

#### **SUBLOCADE™ (BUPRENORPHINE EXTENDED-RELEASE INJECTION) FOR SUBCUTANEOUS USE CIII:**

- In the US:
  - All Post Marketing Requirement (PMR) and Commitment (PMC) studies are on track.
  - Lifecycle Evidence Generation & Optimization (LEGO) Studies: These studies are dedicated to (1) understand the use of diverted buprenorphine (see our publication list); (2) demonstrate that craving could be used as an endpoint to predict illicit opioid use; (3) study the effects of SUBLOCADE™ in the emergency room environment to prevent repeated opioid overdoses and potentially change standards of care, and (4) investigate how high plasma concentrations of buprenorphine, consistent with those delivered by the two approved dosing regimens of SUBLOCADE™, could potentially block the effects of respiratory depression produced by fentanyl that has been increasingly and directly related to drug overdose deaths in the United States. All studies are on track.
  - RECOVER™ Study (REmission from Chronic Opioid use: studying enVironmental and socioEconomic factors on Recovery): This is a study collecting up to 24-month longitudinal data encompassing demographics, drug use, drug treatment, family relationships, quality of life, mental and physical health, health-care utilization, crime, housing, employment, and urine drug screening (see our publication list). The 12-month longitudinal analysis top line findings were made available in December 2018; the 24-month final report is on track for December 2019.
  - Canada: SUBLOCADE™ approval on November 21, 2018
  - SUBLOCADE™ ex-US regulatory filings: Filings were made in Australia (May 2018), Israel (July 2018), New Zealand (September 2018) and Europe (November 2018). Reviews by local Regulatory Authorities are ongoing.

#### **SUBOXONE® (buprenorphine / naloxone) Film:**

- Israel: Submission on September 3, 2018.
- Canada: Supplemental New Drug Submission (SNDS) anticipated in Q2 2019.
- Europe: Market Authorisation Application (MAA – Centralized Procedure) submitted March 8, 2019 and validated on March 28, 2019.

#### **SUBOXONE® (buprenorphine / naloxone) Tablet:**

- On September 11, 2018, the Chinese National Medical Products Administration (NMPA) approved SUBOXONE® Sublingual Tablets for the treatment of opioid use disorder.

- Next Steps: (1) *Scheduling*: Chinese government will complete its narcotic scheduling determination for SUBOXONE® Sublingual Tablets. (2) *Import Permit*: Indivior can apply for the import permit or transfer the Import Drug License (IDL) to a qualified third party.
- On February 4, 2019, Indivior announced a definitive agreement to divest the rights related to SUBOXONE® Sublingual Tablets (Sai Bo Song™) in China to Zhejiang Pukang Biotechnology Co., Ltd. (Pukang) for total potential consideration of up to \$122.5m based on achieving certain development and commercial milestones. The agreement is subject to various closing conditions and is anticipated to close in Q4 2019.

## Treatment of Schizophrenia

- **PERSERIS™ (formerly RBP-7000), Monthly Long-Acting Risperidone Injection:**

- FDA approval on July 27, 2018.
- PMC studies are on track.

## Early Stage Asset Development (ESAD)

- **GABA<sub>B</sub> positive allosteric modulator:**

- Plans to accelerate a new lead identification and optimization program in partnership with ADDEX Therapeutics.

- **C4X3256 (Selective Orexin 1 (OX1) receptor antagonist):**

- NIDA grant in the amount of \$500,000 awarded on June 29, 2018 to assess the efficacy of C4X3256 in reducing the positive reinforcing effect of cocaine in rats that exhibit robust, stable levels of cocaine self-administration.
- Finalization of all preclinical study reports.
- Formulation development and stability work to support First Time In Human (FTIH) studies.
- Finalization of FTIH protocol, Investigators Brochure, Investigational Medicinal Product Dossier.

- **APV202701A (Selective dopamine [DA] D3 receptor antagonist):**

- Initiation of IND dossier preparation.

## Peer-Reviewed Publications (2019)

- Ling W, Nadipelli V, Ronquest N, Albright V, Aldridge A, Learned S, Mehra V, Heidbreder C (2019) Remission from Chronic Opioid Use—Studying Environmental and Socio-economic Factors on Recovery (RECOVER): study design and participant characteristics. *Contemp Clin Trials*, 76: 93-103. <https://doi.org/10.1016/j.cct.2018.11.015>
- Haight BR, Learned SM, Laffont CM, Fudala PJ, Zhao Y, Garofalo AS, Greenwald MK, Nadipelli VR, Ling W, Heidbreder C (2019) Efficacy and safety of a monthly buprenorphine depot injection for opioid use disorder: a multicentre, randomised, double-blind, placebo-controlled trial. *The Lancet*, 393 (10173): 778-790. [https://doi.org/10.1016/S0140-6736\(18\)32259-1](https://doi.org/10.1016/S0140-6736(18)32259-1)
- 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.*, Electronic Publication ahead of Print, March 4. <https://doi.org/10.1097/ADM.0000000000000517>.
- Schmith VD, Curd L, Lohmer LRL, Laffont CM, Andorn A, Young, MA (2019) Evaluation of the effects of a monthly buprenorphine depot subcutaneous injection on qt interval during treatment for opioid use disorder. *Clin Pharmacol Ther*, Epub 2019 Apr 8. <https://doi.org/10.1002/cpt.1406>

## Conference Abstracts (2019)

- Nadipelli, V.R., Solem, C.T., Ronquest, N.A., Yeh, Y.-C., Heidbreder, C., Learned, S.M., Mehra, V. (2019) Impact of BBP-6000 on Patient-reported Outcomes in Patients with Opioid Use Disorder: Results of a Randomized, Placebo-controlled, Phase 3 Study. AMCP Managed Care & Specialty Pharmacy Annual Meeting, March 25-28, San Diego, CA.
- Andorn, A., Haight, B., Greenwald, M.K., Zhao, S., Fox, N.L., Heidbreder, C., Learned, S.M. (2019) Higher Abstinence Rates with Greater Buprenorphine Exposure Among Patients Who Inject Opioids. AMCP Managed Care & Specialty Pharmacy Annual Meeting, March 25-28, San Diego, CA.
- Thompson, S., Andorn, A., Nadipelli, V.R., Graham, J., De Veugh-Geiss, A., Learned, S.M., Heidbreder, C. (2019) The Budget Impact of PERSERIS™: A Once-Monthly Long-Acting Injectable (LAI) Antipsychotic in Patients with Schizophrenia. AMCP Managed Care & Specialty Pharmacy Annual Meeting, March 25-28, San Diego, CA.
- Thompson, S., Andorn, A., Nadipelli, V.R., Graham, J., De Veugh-Geiss, A., Learned, S.M., Heidbreder, C. (2019) The Cost-Effectiveness of PERSERIS™: A Once-Monthly Long-Acting Injectable Antipsychotic in Patients with Schizophrenia. AMCP Managed Care & Specialty Pharmacy Annual Meeting, March 25-28, San Diego, CA.
- Ling, W., Nadipelli, V.R., Ronquest, N., Aldridge, C.T., Solem, N., Peiper, S., Learned, S.M., Heidbreder, C. (2019) Recovery from OUD Following Monthly Extended-Release Buprenorphine Treatment: 12-Month Longitudinal Outcomes. 50<sup>th</sup> Annual Meeting of the American Society of Addiction Medicine (ASAM), April 4-7, Orlando, FL.

- Wiest K, van Velzen M, Algera H, Moss L, Dobbins R. (2019) High therapeutic buprenorphine levels reduce IV fentanyl respiratory depression. Annual Meeting of the American Society of Addiction Medicine (ASAM), April 4-7, Orlando, FL.
- Andorn A, Boyett B, Shinde S, Fox NL, Zhao Y, Learned SM (2019) Long-term RBP-6000, sustained-release buprenorphine for moderate-to-severe OUD. Annual Meeting of the American Society of Addiction Medicine (ASAM), April 4-7, Orlando, FL.
- Wiest K, Andorn A, Fox NL, Learned S, Zhao Y, Gray F (2019) Abstinence response to 300mg vs 100mg RBP-6000 among opioid injection users. Annual Meeting of the American Society of Addiction Medicine (ASAM), April 4-7, Orlando, FL.
- Andorn A, Graham J, Fava M., Csernansky J, Newcomer JW, Walling, D., Shinde S, Muma G, Heidbreder C, (2019) Efficacy of Monthly Extended-release Risperidone Injections (RBP-7000) for the Treatment of Schizophrenia: An Analysis of Individual PANSS Items. Congress of the Schizophrenia International Society's (SIRS), April 10-14, Orlando, FL.