



# FY 2019 UPDATE

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CSO



## TREATMENT OF OPIOID USE DISORDER (OUD)

### SUBLOCADE® (BUPRENORPHINE EXTENDED-RELEASE) INJECTION:

- 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) assess how to induce SUBLOCADE® treatment in the emergency department environment, and (3) 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. All studies are on track.
  - We pursued the analysis of patient-centered outcomes in our Phase III RB-US-13-0001 and RB-US-13-0003 trials. Several manuscripts were submitted and published in peer-reviewed journals (see publication list).
  - The RECOVER™ (REmission from Chronic Opioid Use: Studying EnVironmental and socioEconomic factors on Recovery) study achieved 534 subjects completing 12-month longitudinal analysis. A manuscript was submitted and is currently under peer-review. The final 24-month report was finalised on December 17, 2019 and a peer-reviewed publication is in preparation. The scope and duration of these assessments may lead to important new insights into models of recovery and allow researchers, clinicians, and patients to more accurately characterize the process of recovery, identify factors that promote or hinder success, and potentially develop new and personalized treatment strategies. In order to strengthen this approach, Indivior [announced](#) a new partnership with the Virginia Polytechnic Institute and State University (Virginia Tech).
- Ex-US Regulatory Activities:
  - Canada: SUBLOCADE® approval on November 21, 2018.
  - Australia: SUBLOCADE® approval on July 17, 2019.
  - Ex-US regulatory filings: Filings were made in Israel (July 2018), New Zealand (September 2018) and Europe (November 2018). Reviews by local Regulatory Authorities are ongoing.

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

- Canada: Supplemental New Drug Submission (SNDS) filed June 27, 2019; Screening acceptance letter received September 23, 2019. Regulatory Authority review is ongoing.
- Europe: Market Authorisation Application (MAA – Centralized Procedure) submitted March 8, 2019 and validated on March 28, 2019. Regulatory Authority review is ongoing.

- Israel: Submission on September 3, 2018. Regulatory Authority review is ongoing.
- New Zealand: Regulatory dossier submitted October 30, 2019. Regulatory Authority review is ongoing.
- Middle East: Regulatory dossier submissions in Kingdom of Saudi Arabia, United Arab Emirates, Qatar and Kuwait are planned for 2020 pending registration agreement with local distributors.

### **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.
- 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. The agreement is subject to various closing conditions (ongoing).

### **TREATMENT OF SCHIZOPHRENIA**

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

- FDA approval on July 27, 2018.
- PMC studies on track.
- Canada: HLS Therapeutics and Indivior held an Integration kick-off meeting on June 14, 2019. The NDS was submitted to Health Canada on November 7, 2019. Regulatory review is ongoing.

### **EARLY STAGE ASSET DEVELOPMENT (ESAD)**

#### **• GABA<sub>B</sub> positive allosteric modulator:**

- New lead identification and optimization program is [ongoing](#) in partnership with ADDEX Therapeutics.

#### **• C4X3256 (Selective Orexin 1 (OX1) receptor antagonist):**

- On September 26, 2019 the National Institutes of Health (NIH) granted Indivior's application entitled "*Clinical Evaluation of C4X3256, a Non-Opioid, Highly-Selective Orexin-1 Receptor Antagonist for the Treatment of Opioid Use Disorder*" pursuant to Funding Opportunity Announcement RFA-DA-19-002 dedicated to the development of medications to prevent and treat opioid use disorder and overdose. A link to Indivior's Press Release can be found [here](#).
- A pre-investigational new drug application (PIND) application was submitted to the FDA on September 20, 2019. FDA feedback was received on January 2,

2020. First-In-Human protocol has now been finalized and the IND was filed on January 17, 2020.

- Our development plans were presented at the first [HEAL Investigator Meeting](#) in Bethesda on January 16-17, 2020.
- **APV202701A (Selective dopamine [DA] D3 receptor antagonist):**
  - Initiation of IND-related activities and dossier preparation in partnership with Aptuit.

## PEER-REVIEWED PUBLICATIONS (2019)

1. 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>
2. 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)
3. Ling W, Nadipelli VR, Solem CT, Ronquest NA, Yeh Y-C, Learned SM, Mehra V, Heidbreder C (2019) Patient-Centered 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://www.ncbi.nlm.nih.gov/pmc/articles/PMC6844648/>
4. 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. *Clinical Pharmacology & Therapeutics*, 106(3): 576-584. <https://doi.org/10.1002/cpt.1406>
5. Berrell SL, Stephen J, Byard SJ, John S, Carey JS, Antonio Codina A, J. Alf Davis JA, Katherine Filer K, Alasdair Garnett A, Robin Marshall R, Martin SJ, Mykytiuk J, Northen J, Pandya U, Reid G, Smyth C, Watson (2019) Process Development toward a Pro-Drug of Buprenorphine. *Organic Proc Res & Dev*, 23(5): 762-770. <https://doi.org/10.1021/acs.oprd.9b00025>
6. Carey JS and McCann E (2019) Lipase-Catalyzed Regioselective Ester Hydrolysis as a Key Step in an Alternative Synthesis of a Buprenorphine Pro-Drug. *Organic Process Res & Dev*, 23(5): 771-774. <https://doi.org/10.1021/acs.oprd.9b00026>
7. Ling W, Nadipelli VR, Solem CT, Farabee D, Ronquest NA, Perrochet B, Learned SM, Deshpande CG, Heidbreder C (2019) Measuring recovery in OUD: clinical utility and psychometric properties of the treatment effectiveness assessment. *Subst Abuse Rehabil*, 10: 13-21. <https://doi.org/10.2147/SAR.S198361>
8. Dong R, Wang H, Lang L, Gray F, Liu Y, Laffont C, Young M, Jiang J, Liu Z, Learned SM (2019) Pharmacokinetics of sublingual buprenorphine tablets following single and multiple doses in Chinese participants with and without opioid use disorder. *Drugs in R&D*, 19(3): 225-265. <https://doi.org/10.1007/s40268-019-0277-9>
9. Chilcoat HD, Amick HR, Sherwood, MR, Dunn KE (2019) Buprenorphine in the United States: motives for abuse, misuse, and diversion. *J Subst Abuse Treat*, 104: 148-157. <https://doi.org/10.1016/j.jsat.2019.07.005>
10. Dhanda R, Varghese D, Nadipelli VR, Fava M, Joshi N, Solem C, Graham J, Learned SM, Heidbreder C (2019) Patient-reported outcomes in schizophrenia patients treated with once-monthly extended-release risperidone in a long-term clinical study. *Patient Preference & Adherence*, 2019(13): 1037-1050. <https://doi.org/10.2147/PPA.S202173>

11. Andorn A, Graham J, Csernansky J, Newcomer JW, Shinde S, Muma G, Heidbreder C, Fava M (2019) Monthly Extended-release Risperidone (RBP-7000) in the Treatment of Schizophrenia: Results from the Phase 3 Long-term Open-Label Study. *J Clin Psychopharmacol*, 39(5): 428-433.  
<https://doi.org/10.1097/JCP.0000000000001076>
12. Kakko J, Alho H, Baldacchino A, Molina R, Nava F, Shaya G (2019) Craving in opioid use disorder: from neurobiology to clinical practice. *Front Psychiatry*, 10:592. <https://doi.org/10.3389/fpsy.2019.00592>
13. Ling, W, Nadipelli, V.R., Solem, C.T., Ronquest, N.A, Yeh, Y.-C., Learned, S.M., Mehra, V. Heidbreder, C. (2020) Effects of Monthly Buprenorphine Extended-release Injections on Patient-centered Outcomes: A Long-term Study. *Journal of Substance Abuse Treatment*. *J Subst Abuse Treat*, 110: 1-8.  
<https://doi.org/10.1016/j.jsat.2019.11.004>

### **CONFERENCE ABSTRACTS (2019)**

1. Nadipelli VR, Solem CT, Ronquest NA, Yeh Y-C, Heidbreder C, Learned SM, Mehra V (2019) Impact of RBP-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.
2. Andorn A, Haight B, Greenwald MK, Zhao S, Fox NL, Heidbreder C, Learned SM (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.
3. Thompson S, Andorn A, Nadipelli VR, Graham J, De Veugh-Geiss A Learned SM, 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.
4. Thompson S, Andorn A, Nadipelli VR, Graham J, De Veugh-Geiss A, Learned SM, 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.
5. Ling W, Nadipelli VR, Ronquest N, Aldridge A, Solem CT, Peiper N, Learned SM, Heidbreder C (2019) Recovery from OUD Following Monthly Extended-Release Buprenorphine Treatment: 12-Month Longitudinal Outcomes. 50th Annual Meeting of the American Society of Addiction Medicine (ASAM), April 4-7, Orlando, FL.
6. 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.
7. 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.

8. 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.
9. 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.
10. Andorn A, Graham J, Csernansky J, Newcomer JW, Shinde S, Muma G, Heidbreder C, Fava M (2019) Efficacy of Monthly Extended-release Risperidone Injections (RBP-7000) for the Treatment of Schizophrenia: Comparison of Two Analyses. 172nd Annual Meeting of the American Psychiatric Association (APA), May 18-22, San Francisco, CA.
11. Andorn A, Boyett B, Shinde S, Fox NL, Zhao S, Learned S (2019) 18-month Safety and Efficacy of RBP-6000 Extended-release Buprenorphine for OUD. ALBATROS - 13th Congrès International d'Addictologie (ALBATROS), June 5-7, 2019, Paris, France.
12. Fox NL, Laffont CM, Zhao S, Gray F, Andorn A, Learned SM, Heidbreder C (2019) Risk-Adjusted Abstinence Rates are Higher with Greater Buprenorphine Plasma Exposure Among Patients Who Inject Opioids. 81st Annual Scientific Meeting of the College on Problems of Drug Dependence (CPDD), June 15-19, San Antonio, TX.
13. Ling W, Nadipelli VR, Ronquest N, Aldridge CT, Solem N, Peiper S, Learned SM, Heidbreder C (2019) How Long Should Pharmacotherapy Last for the Treatment of Opioid Use Disorder? Evidence from a 12-Month Observational Study. 81st Annual Scientific Meeting of the College on Problems of Drug Dependence (CPDD), June 15-19, San Antonio, TX.
14. Chilcoat HD, Amick HR, Sherwood MR, Dunn KE (2019) Buprenorphine in the United States: motives for misuse, abuse, and diversion. 81st Annual Scientific Meeting of the College on Problems of Drug Dependence (CPDD), June 15-19, San Antonio, TX.
15. DeVeaugh-Geiss AM, Chilcoat HM (2019) Buprenorphine use and misuse among those with opioid use disorders with and without recent treatment. 81st Annual Scientific Meeting of the College on Problems of Drug Dependence (CPDD), June 15-19, San Antonio, TX.
16. Moss LM, Algera MH, van Velzen M, Heuberger J, Strafford S, Gray F, Dobbins R, Dahan A, Groeneveld G (2019) High therapeutic buprenorphine levels reduce IV fentanyl respiratory depression. Nederlandse Vereniging voor Toxicologie (NVT) - 2019 Annual Meeting, June 12-13, Ede, Netherlands.
17. Roncero C, Dorado ML, Orenge T, Ortega RL, Palma-Álvarez RF, Yébenes M, Ordovás M, Grau-López L (2019) Direct healthcare costs for the management of patients with Opioid Use Disorder treated with methadone and

buprenorphine/naloxone in Real-World setting in Spain. COSTEDOPIA Study. World Association on Dual Disorders (WADD) - 3rd World Congress, June 19-22, Madrid, Spain.

18. Simmel B, Ling W, Nadipelli V, Ronquest N, Aldridge A, Solem C, Peiper N, Learned S, Heidbreder C (2019) Recovery from OUD Post Monthly Buprenorphine-XR Treatment: 12-Month Longitudinal Outcomes. Interdisziplinärer Kongress für Suchtmedizin -20th (IKS), July 4-6, Munich, Germany.
19. Simmel B, Andorn A, Boyett B, Shinde S, Fox NL, Zhao Y, Learned S (2019) Recovery from OUD Post Monthly Buprenorphine-XR Treatment: 18-month Safety and Efficacy of RBP-6000 Extended-release buprenorphine for OUD. Interdisziplinärer Kongress für Suchtmedizin -20th (IKS), July 4-6, Munich, Germany.
20. Farah M, Ling W, Nadipelli VR, Ronquest NA, Aldridge AP, Solem CT, Peiper NC, Learned SM, Heidbreder C (2019) Recovery from OUD Post-Monthly Buprenorphine-XR Treatment: 12-Month Longitudinal Outcomes. Addictions Toxicomanies Hepatites SIDA - 14th Colloque International (ATHS), Oct 1-4, Biarritz, France.
21. Farah M, Andorn AC, Boyett B, Shinde S, Fox NL, Zhao Y, Learned SM (2019) 18-month Safety and Efficacy of RBP-6000 Extended-release Buprenorphine for OUD. Addictions Toxicomanies Hepatites SIDA - 14th Colloque International (ATHS), Oct 1-4, Biarritz, France.
22. Albright VA, Aldridge AP, Heidbreder C, Learned SM, Ling W, Mehra V, Peiper NC, Ronquest NA, Solem CT (2019) What Is the Optimal Duration of Treatment in Opioid Use Disorder? Addictions Toxicomanies Hepatites SIDA - 14th Colloque International (ATHS), Oct 1-4, Biarritz, France.
23. Andorn A, Graham JA, Fava, Csernansky, Newcomer JW, Walling DP, 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. US Psych Congress, Oct 3-6, San Diego, California.
24. Nava FA, Wiest K, Algera MH, Moss L, van Velzen M, Groeneveld GY, Heuberger J, Dahan A, Gray F, Strafford S, Dobbins R (2019) High Therapeutic Buprenorphine Plasma Levels Reduce Respiratory Depression induced by IV Fentanyl. Federazione Italiana degli Operatori dei Dipartimenti e dei Servizi delle Dipendenze (FeDeSeRD), Oct 9-11, Firenze, Italy.
25. Andorn AC, Boyett B, Shinde S, Fox NL, Zhao Y, Learned SM (2019) 18-month Safety and Efficacy of RBP-6000 Extended-release Buprenorphine for OUD. Canadian Society for Addiction Medicine (CSAM), Oct 24-27, Halifax, Canada.
26. Wiest K, Algera MH, Moss L, van Velzen M, Dobbins R (2019) High Therapeutic Buprenorphine Levels Reduce IV Fentanyl Respiratory Depression. Canadian Society for Addiction Medicine (CSAM), Oct 24-27, Halifax, Canada.
27. Ling W, Nadipelli VR, Ronquest NA, Aldridge AP, Solem CT, Peiper NC, Learned SM, Heidbreder C (2019) Recovery from OUD Post-Monthly Buprenorphine-XR Treatment: 12-Month Longitudinal Outcomes. Canadian Society for Addiction Medicine (CSAM), Oct 24-27, Halifax, Canada.



28. Ling W, Nadipelli VR, Ronquest NA, Aldridge AP, Solem CT, Peiper NC, Learned SM, Heidbreder C (2019) Recovery from OUD Post-Monthly Buprenorphine-XR Treatment: 12-Month Longitudinal Outcomes. Academy of Managed Care Pharmacy - 7th Nexus Conference (AMCP Nexus), Oct 29-Nov 1, National Harbor, MD.
29. Fox NL, Laffont C, Zhao S, Gray F, Andorn A, Learned S, Heidbreder C (presented by Barbara Simmel) (2019) Risk-Adjusted Abstinence Rates are Higher with Greater Buprenorphine Plasma Exposure Among Patients Who Inject Opioids. Deutsche Gesellschaft für Suchtmedizin - 28th Congress (DGS), Nov 1-3, Berlin, Germany.
30. Wiest K, Algera MH, Moss L, van Velzen M, Jan Groeneveld G, Heuberger J, Dahan A, Gray F, Strafford S, Dobbins R (presented by Barbara Simmel) (2019) High Therapeutic Buprenorphine Levels Reduce IV Fentanyl Respiratory Depression. Deutsche Gesellschaft für Suchtmedizin - 28th Congress (DGS), Nov 1-3, Berlin, Germany.
31. Roncero C, Dorado ML, Orengo T, Ortega RL, Palma-Álvarez RF, Munoz A, Casado MA, Grau-López L, Ahuir J (2019) Direct healthcare costs for the management of patients with Opioid Use Disorder treated with methadone and buprenorphine/naloxone in Real-World setting in Spain. COSTEDOPIA Study. International Society for Pharmacoeconomics and Outcomes Research - 22nd Annual European Congress (ISPOR) Nov 2-6, Copenhagen, Denmark.
32. Ling W, Nadipelli VR, Ronquest NA, Aldridge AP, Solem CT, Peiper NC, Learned SM, Heidbreder C (2019) Recovery from OUD Post-Monthly Buprenorphine-XR Treatment: 12-Month Longitudinal Outcomes. Svenska Foreningen for Alkohol-och Drogforskning/Svenska Forening for Beroendemedicin - 7th Forskningsmote (SAD/SFB), Nov 7-8, Skovde, Sweden.
33. Andorn A, Boyett B, Shinde S, Fox NL, Zhao S, Learned S (2019) 18-month Safety and Efficacy of RBP-6000 Extended-release Buprenorphine for OUD. Svenska Foreningen for Alkohol-och Drogforskning/Svenska Forening for Beroendemedicin - 7th Forskningsmote (SAD/SFB), Nov 7-8, Skovde, Sweden.
34. Ling W, Nadipelli VR, Ronquest NA, Aldridge AP, Solem CT, Peiper NC; Learned SM, Heidbreder C (2019) Recovery from OUD Post-Monthly Buprenorphine-XR Treatment: 12-Month Longitudinal Outcomes. Society for the Study of Addiction - 2019 Annual Symposium (SSA), Nov 7-8, Newcastle, UK.
35. Wiest K, Algera H, Moss L, van Velzen M, Dobbins R, Heuberger J, Jan Groeneveld G, Dahan A, Gray F, Strafford S (2019) High Therapeutic Buprenorphine Levels Reduce IV Fentanyl Respiratory Depression. Society for the Study of Addiction - 2019 Annual Symposium (SSA), Nov 7-8, Newcastle, UK.
36. Larance B, Degenhardt L, Grebely J, Nielsen S, Bruno R, Dietze P, Lancaster K, Larney S, Santo T, Shanahan M, Memedovic S, Ali R, Farrell M (2019) Perceptions of extended-release buprenorphine injections for opioid dependence: A cross-sectional survey of people who use opioids regularly conducted prior to implementation in Australia. Australasian Professional Society on Alcohol and other Drugs - 39th Conference (APSAD), Nov 10-13, Hobart, Australia.
37. Andorn A, Boyett B, Shinde S, Fox NL, Zhao Y, Learned S (2019) 18-month Safety and Efficacy of RBP-6000 Extended-release Buprenorphine for opioid use

disorder. Australasian Professional Society on Alcohol and other Drugs - 39th Conference (APSAD), Nov 10-13, Hobart, Australia.