Q1-2022 RESULTS
R&D UPDATE

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TREATMENT OF OPIOID USE DISORDER (OUD)

SUBLOCADE® (BUPRENORPHINE EXTENDED-RELEASE) INJECTION (US)

- US Label updates:
  - → *N-methyl-pyrrolidone (NMP) safety:* Proposed label reviewed by FDA and responses sent back to the Agency on April 4, 2022. Pending.
  - → *Thorough QT (tQT) labeling information:* The FDA provided (March 31, 2022) a Safety Labelling Change (SLC) notification to harmonize the QTc information in all buprenorphine labels, including SUBLOCADE.
- Post Marketing Requirement study (INDV-6000-401): (1) Identify the population of patients who may benefit from the 300 mg/month maintenance regimen; (2) Demonstrate that initiating SUBLOCADE® 300 mg following a single 4 mg dose of transmucosal buprenorphine is well-tolerated with a safety profile similar to that observed with SUBLOCADE® administered as per current FDA label; (3) Assess feasibility of fast 300 mg loading induction for the most vulnerable patients. First subject randomized on December 23, 2021. Study ongoing.
- Lifecycle Management Plan: Generate further evidence on how to (1) use SUBLOCADE® in fentanyl and synthetic opioids' users: (2) treat subjects with opioid use disorder (OUD) in the criminal justice system to potentially decrease the risk of overdose after release and improve linkage to care, and (3) initiate treatment in the emergency department to potentially decrease the rates of relapse and overdose and facilitate transitions to community-based care. All studies in planning phase.
- Collaboration studies:
  - → *RECOVER® long-term study*: Extension of RECOVER® study to provide a multidimensional (e.g., substance use, psychosocial and physiological outcomes, temporal reward preference) understanding of recovery from OUD at an average of 4.2 years post-participation in SUBLOCADE® pivotal Phase 3 clinical trial.[1]
  - → *Real world Australian experience with SUBLOCADE®*: COLAB study, an open-label, multicentre, single-arm trial of monthly injections of SUBLOCADE® in people with OUD.[2]
  - → *Real world Canadian experience with SUBLOCADE®*: Distribution of reported non-fatal overdose events by month & treatment cohort.[3]
  - → *EU EXPO study*: First prospective randomized comparison of SUBLOCADE® with standard of care (SL buprenorphine/naloxone and methadone).

SUBUTEX® PROLONGED-RELEASE SOLUTION FOR INJECTION (ex-US):

- Regulatory approvals granted in 10 countries including Canada, Australia, New Zealand, Israel, Sweden, Finland, Denmark, Norway, Germany, and Italy.
- Marketing Authorisation Application in Switzerland deemed approvable. Waiting for MHRA feedback in the UK.

SUBOXONE® (BUPRENORPHINE / NALOXONE) FILM:

- Regulatory Approvals granted in Canada, Israel, all EU Member States (+ UK, Iceland, Norway, and Liechtenstein), New Zealand, Qatar and United Arabic Emirates.
- Filings under review in Kuwait and Kingdom of Saudi Arabia. Filed in Colombia.

TREATMENT OF SCHIZOPHRENIA

PERSERIS™ ONCE MONTHLY RISPERIDONE FOR EXTENDED-RELEASE INJECTABLE SUSPENSION:

- Alternate injection site prior approval supplement (PAS): Submitted to FDA on February 15, 2022. Anticipated approval Q4-2022.

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[1] *Craft W et al. (2022) Recovery from opioid use disorder: a 4-year post-clinical trial outcomes study. Drug Alcohol Depend. Mar 9;234:109389. https://doi.org/10.1016/j.drugalcdep.2022.109389*

[2] *Farrell M et al. (2022) Outcomes of a single-arm implementation trial of extended-release subcutaneous buprenorphine depot injections in people with opioid dependence. Int J Drug Policy, 100: 103492. https://doi.org/10.1016/j.drugpo.2021.103492*

[3] *Lee et al. (2021) Real-World Evidence for the Management of Opioid Use Disorder (OUD) During COVID-19 pandemic for patients receiving Opioid Agonist Treatment (OAT), CSAM, October 21-23, 2021*

- Extension of shelf-life and time out of fridge PAS: Submission to FDA in May 2022. Anticipated approval Q4-2022.

PIPELINE ACTIVITIES

- **AEF0117 (Cannabinoid-1 [CB1] synthetic Signalling Specific Inhibitor):**
  - Phase IIb clinical study: central IRB approval and global protocol training achieved on March 30, 2022. First subject first visit April 2022.
  - Other CMC, nonclinical toxicology and clinical workstreams are progressing in parallel as planned.
- **INDV-2000 (Selective Orexin 1 [OX1] receptor antagonist):**
  - FDA clinical hold letter received September 1, 2021, asking Indivior to conduct an additional 28-day repeat-dose toxicology study. FDA's decision was based on non-clinical findings from a separate (not sponsored by Indivior) development program.
  - Final toxicology study report expected for end of Q2-2022 pending availability of full histopathology reports. Data package to be submitted to FDA for review of clinical hold as soon as available to re-initiate multiple ascending dose (MAD) study in Q3-2022.
- **INDV-1000 ($GABA_B$ receptor positive allosteric modulator):**
  - Two lead molecules and potential backups have been chosen for the late lead optimization phase.
  - Ongoing synthesis of the two lead molecules to enable Maximum Tolerated Dose (MTD) / Dose Range Finding (DFR) rat and dog studies.

PEER-REVIEWED PUBLICATIONS (2022)

1. Moss LM et al. (2022) Effect of Sustained High Buprenorphine Plasma Concentrations on Fentanyl-Induced Respiratory Depression: A Placebo-Controlled Crossover Study. PlosOne, Published online January 27, 2022. https://doi.org/10.1371/journal.pone.0256752
2. Craft W et al. (2022) Recovery from opioid use disorder: a 4-year post-clinical trial outcomes study. Drug Alcohol Depend. Mar 9;234:109389. https://doi.org/10.1016/j.drugalcdep.2022.109389
3. Olofsen E. et al. (2022) Modelling Buprenorphine Mitigation of Fentanyl-Induced Respiratory Depression in Chronic Opioid Users and Opioid-Naïve Volunteers. JCI Insight. https://doi.org/10.1172/jci.insight.156973

CONFERENCE ABSTRACTS (2022)

1. Abdel-Sattar M et al. (2022) Provider and Payer Perspectives on the Impact of the COVID-19 Pandemic on Patients With Opioid Use Disorder in the United States: Multi-Stakeholder In-Depth Interviews, AMSUS (The Society of Federal Health Professionals), February 7-10, 2022 (Virtual February 22-25).
2. Carey J et al. (2022) The Identification of Naloxone Related Degradants in Drug Product, 38th SCI Process Development Symposium, Society of Chemical Industry (SCI), March 30 – 31, 2022, London, UK.
3. Rutrick D et al. (2022) Long-Term Treatment Benefit of BUP-XR for Patients Struggling to Abstain from Opioid, American Society of Addiction Medicine (ASAM), March 31-April 3, 2022, Hollywood, FL.
4. Gaiazov S et al. (2022) Mental Health and its relationship to Economic Stability, Education, Health and Treatment Facilities: A State-level analysis. Spring Conference on Correctional Health Care (NCCHC), April 9-12, 2022, Atlanta, GA.
5. Gaiazov et al. (2022) Recognizing the Role of Socioeconomic Geography in the Distribution of Waivered Providers. The College of Psychiatric and Neurologic Pharmacists (CPNP), April 24-27, San Antonio, TX.