

("C4XD", "C4X Discovery" or the "Company")

### **Business Update**

*Continued progress across proprietary portfolio*

*Phase 1 clinical trial with C4X\_3256 initiated by partner Indivior*

*New Taxonomy3<sup>®</sup> collaboration with the GEN-COVID Consortium, Italy, to examine COVID-19 genetics*

**25 August 2020** – C4X Discovery Holdings plc (AIM: C4XD), a pioneering Drug Discovery company, today provides a business update.

#### **Clive Dix, CEO of C4XD, commented:**

*"I am delighted to share the progress we have made over recent months across our proprietary portfolio despite the challenges of the COVID-19 pandemic, in particular, the continued headway in our key inflammation programmes. Importantly, Indivior recently commenced a Phase 1 clinical trial with our selective Orexin-1 antagonist, C4X\_3256, for the treatment of opioid dependence and we eagerly await those results in due course. Our two most advanced programmes, NRF-2 and IL-17, continue to move forward with one of our lead NRF-2 molecules, C4X\_6746, showing significant efficacy in a pre-clinical model of Inflammatory Bowel Disease (IBD). This enables expansion of our commercial discussions beyond those partners already engaged in assessing the programme for Pulmonary Arterial Hypertension and Sickle Cell Disease.*

*"We are also pleased to announce a new partnership with the GEN-COVID Consortium in Italy. The collaboration will utilise Taxonomy3<sup>®</sup> to examine genetic data from a significant number of COVID-19 patients to identify genes specifically associated with severe COVID-19 disease. The disease continues to spread throughout the world and a clear understanding of how it affects people differently remains elusive. We believe that genetics may play a role in explaining the differences in an individual's disease susceptibility, severity and prognosis. This is a new area for C4XD and we are excited to be working on such an important project. We remain committed to deliver and drive novel small molecule drugs against challenging targets towards clinical development."*

C4XD has continued to make progress across key programmes in its portfolio:

- Indivior has commenced a Phase 1 clinical trial for C4XD's novel selective Orexin-1 antagonist, C4X\_3256 (also known as INDV-2000), for the treatment of opioid dependence with the first patient now dosed (<https://www.clinicaltrials.gov/ct2/show/NCT04413552>). This single ascending dose study in healthy volunteers is anticipated to complete by year end.
- One of C4XD's lead NRF-2 activator molecules C4X\_6746, has recently been shown to significantly inhibit the disease score in a pre-clinical model of IBD in a dose-related manner. Candidate nomination studies continue.
- The lead optimisation stage has been initiated for C4XD's novel oral IL-17 inhibitor programme for the treatment of Psoriasis with the aim of identifying further improved small molecules to drive towards a pre-clinical candidate shortlist. We note that Leo Pharma A/S has recently announced that it has identified the first oral IL-17 inhibitor IND-ready candidate with clinical studies expected to be initiated soon. This provides further confidence that the challenge of developing a small molecule alternative to injectable monoclonal antibodies to target IL-17 can be achieved and there has been increased interest from potential pharma partners.



- Significant progress has been made on C4XD's early oral inhibitor programme targeting  $\alpha 4\beta 7$  integrin for the treatment of IBD. Effective antibody therapy against this target is already approved, removing the clinical target risk, but effective oral therapy remains highly sought after. C4XD has identified a second series of novel, potent and selective inhibitors providing a further competitive edge for this programme. This reaffirms the capability of C4XD's Conformetrix technology to discover novel chemical scaffolds for high-value challenging drug targets. Both series have recently demonstrated oral bioavailability in PK studies with the current focus on improving PK properties to demonstrate functional inhibition of  $\alpha 4\beta 7$  integrin *in vivo* following oral dosing.
- The LifeArc risk-share collaboration on an oral small molecule inhibitor programme for the treatment of haematological cancers and inflammatory disease continues to progress well despite being impacted by COVID-19. Three novel series have been identified by harnessing C4XD's Conformetrix technology and recent data has demonstrated functional cell activity and oral bioavailability for all three series. Optimisation continues with the aim of demonstrating functional inhibition of the target *in vivo* following oral dosing.
- C4XD has recently entered a new collaboration with the GEN-COVID consortium, a network of more than 20 hospitals in Italy led by Professor Alessandra Renieri of the University of Siena. The collaboration will use the unique mathematical genetic analysis methodology of Taxonomy3<sup>®</sup> to investigate the role genetics plays in the widely varied disease susceptibility, severity and prognosis observed between individuals with COVID-19. Taxonomy3<sup>®</sup> will analyse genetic data from a significant number of COVID-19 positive patients collected by the consortium to identify genes associated with severe COVID-19 disease. The aim is to identify a unique genetic signature that can successfully predict mild vs. severe disease to inform treatment of patients at risk. The analysis may also uncover novel biology driving severity of the disease which may inform potential novel drug targets for treatment.

- Ends -

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## Notes to Editors:

### **About C4X Discovery**

C4X Discovery (C4XD) aims to create the world's most productive Drug Discovery engine by using cutting-edge technologies and expertise to efficiently deliver best-in-class small-molecule medicines to clinical partners for the benefit of patients. The Company's business model focuses on replenishing big pharma discovery pipelines and driving returns through revenue generating pre-clinical licensing deals. In 2018, C4XD successfully out-licensed a pre-clinical programme in addictive disorders to Indivior in a deal worth up to \$294m.



C4XD has a state-of-the-art suite of proprietary technologies across the Drug Discovery process and accesses further innovative capabilities and expertise through its growing network of partners. The Company is actively advancing its diverse pre-clinical discovery portfolio which is focused on inflammation, neurodegeneration and oncology (including immuno-oncology). Opportunities to maximise value from the portfolio are proactively driven by C4XD's commercial division. The Company is led by a highly experienced management team and Board who have delivered significant value creation within the healthcare sector.

#### **About Taxonomy3®**

Taxonomy3® is a novel in silico platform technology that utilises proprietary ground-breaking mathematical algorithms to perform complex multivariate analysis of genetic data. Since these novel targets are based on human genetic data, this enables the discovery of targets that cause disease, rather than those that are simply associated with its symptoms, and thereby provides the best starting point for drug discovery, biomarker identification and patient stratification. The resulting drugs have a greater probability of successful clinical development and product realisation.

For additional information please go to: [www.c4xdiscovery.com](http://www.c4xdiscovery.com)

#### **About GEN-COVID**

GEN-COVID is a network of more than 20 Italian Hospitals led by Professor Alessandra Renieri of the University of Siena in Italy. The network started its activity on March 16, 2020 after IRB approval and it is collecting samples from 2,000 patients, in order to develop a genetic-based approach to understand the clinical variability of COVID-19 public health emergency.

For additional information please go to: <https://sites.google.com/dbm.unisi.it/gen-covid>