# Antiviral drug development: Hits to Leads

CARE — CORONA ACCELERATED R&D IN EUROPE

## Leads

**Patrick Chaltin**
**CD3 (KULeuven)**
**& CISTIM**
Academic Lead

**Nico Bräuer**
**NUVISAN**
Industry Lead

## Objectives

- Identify 2-3 effective, safe, oral preclinical development candidates with broad-spectrum coronavirus activity
- Develop a streamlined and efficient drug discovery testing cascade for coronaviruses to support rapid profiling and triaging compounds
- Develop a rapid and effective fully integrated medicinal chemistry/computation approach and strategy to optimise compounds
- Assess the impact of small molecules R&D decisions on the downstream health system, focus on pandemic preparedness and outbreak response up to the point of care delivery

## CONNECTIONS
### *with other work packages*

**Work package 1**
Screening of compound libraries from WP3 to identify antiviral hit compounds; antiviral activity testing & characterization, incl mode of action studies for compounds from WP3

**Work package 2**
Evaluating compounds from WP3 in target-based assays for hit identification, compound optimisation and characterization; structural biology (cryo-EM, X-ray crystallography) with compounds of interest from WP3

**Work package 6**
Animal models: evaluation of in vivo activity of WP3 compounds

## BREAKTHROUGH *moments*

**2021** — **CD3/KU Leuven:** SubµM antiviral potency followed by target identification (resistance selection)

**2022** — **Ai-biopharma:** identified first hit series
**CD3/KU Leuven:** animal proof of concept in two compound series
**University of Dundee:** ligand-bound crystal structure obtained
**Nuvisan**: Sub µM potency

**2023** — **Ai-biopharma:** first lead family confirmed
**CD3/KU Leuven:** Cryo-EM structure with representative compound
**Nuvisan**: Animal PoC achieved
**KU Leuven**: Conceptual impact model

**2024** — **Nuvisan**: Target confirmed

## PUBLIC DELIVERABLES

**D3.1 Drug discovery testing cascade for CoVs**
**D3.2-3.3 Optimised leads 1 & 2**
**D3.4 Coordinated AI-platform**
**D3.5-3.7 System impact model – conceptual /quantitative/system maps**
**D3.8 Analysis of targets for druggability**
**D3.9-3.12 Periodic portfolio reports**

## KEY STATISTICS

| | |
|---|---|
| Hits investigated | **>50** |
| Compounds synthesized by WP3 partners | **>4000** |
| Compound series with a novel mode of action identified | **5** |
| Compound series in lead optimization towards new potential candidate drugs | **4** |

## Partner Organisations

CD3 | CENTRE FOR DRUG DESIGN AND DISCOVERY · NUVISAN · University of Dundee · Takeda · KU LEUVEN · Cistim · Ai-biopharma · Pfizer · UNIVERSITÄT ZU LÜBECK · UNIWERSYTET JAGIELLOŃSKI W KRAKOWIE · Universität Hamburg · Boehringer Ingelheim · GHDDI · IKTOS · Exscientia · Merck · BILL & MELINDA GATES foundation