

Perspectives on advancing the field of the early and late-stage development of antivirals

HERA-AVITHRAPID Workshop
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AVITHRAPID
PROJECT

Fact about the SARS–CoV2 Pandemic

- Globally we were not ready to share data regarding the spread of the pandemic, the correct method to monitor the infections, the understanding of the pathogen and the possible medications
- There was not effective coordination among the WHO and the National and local Health Institutions
- Each Nation took several months to organize both the monitoring and the treatments, the lockdown was the most reasonable choice
- The drug repurposing approaches were not very efficient
- The discovery of new therapeutic agents were also too slow
- The vaccines were a challenge but were incredible useful
- The mRNA vaccines were the greatest technology finally validate to produce vaccine

**In conclusions, we were poorly organized globally and locally,
i.e. unprepared to give an immediate response**

What did we learn from the SARS CoV-2 Pandemic ?

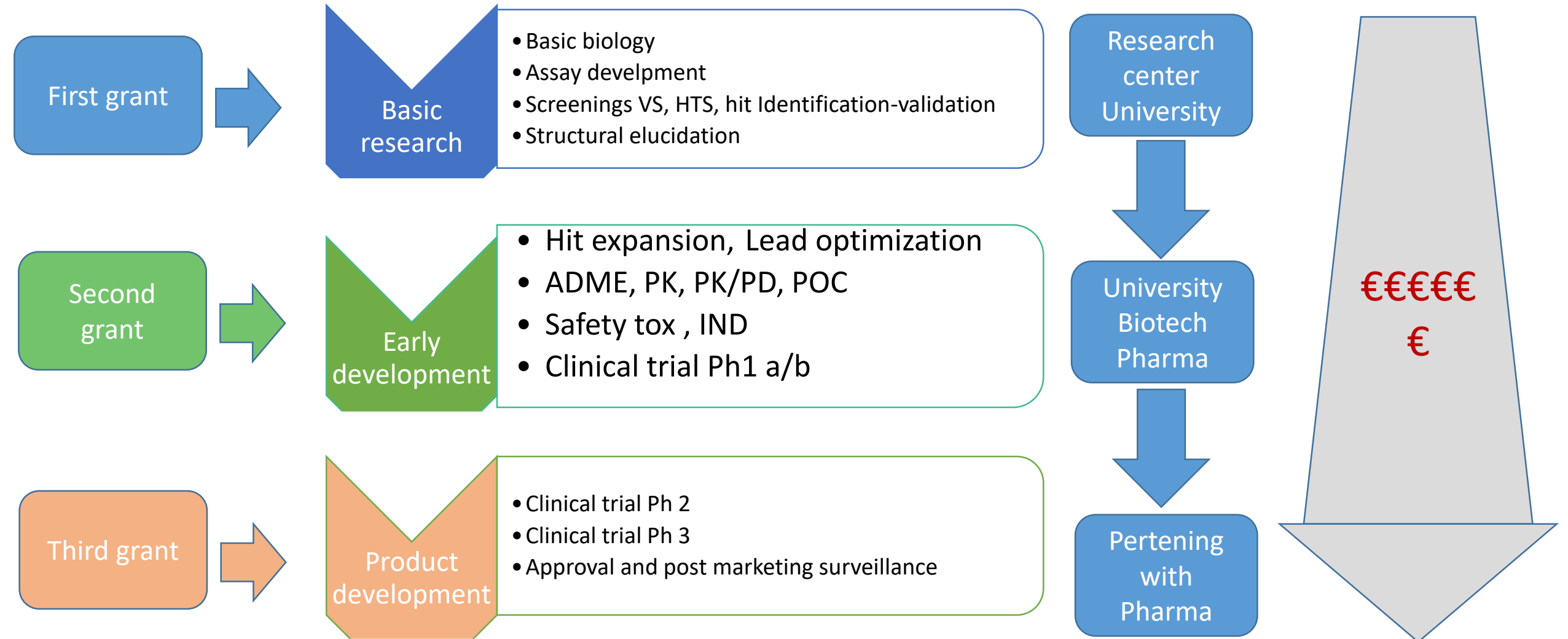
Needs:

- An independent organization designated to monitor, collect and share data continuously on the spread of new infection at global and local level

Invest constantly, even if there is no immediate risk of pandemics, in:

- basic research regarding the biology and transmission of the pathogens with high pandemic potential
- **Work very hardly on the already known conserved targets to identify pan- inhibitors**
- Identify new pathogen targets that are highly conserved across the same family
- Potentiate and validate the AI in generating and analyzing the putative evolution of pathogen targets
- Potentiate the structural biology on the pathogen targets to have not only homology model of the pathogen targets for the inhibitors design
- Understanding host-pathogen interactions, and the immune response

What should we do to be very effective in advancing the antiviral field?



AVITHRAPID case of study: objectives aligned with HERA

1 Supporting pandemic preparedness by provision of novel approaches for the development of antivirals

2 Development of novel broad-spectrum antivirals providing additional therapeutic options for current and future epidemics and pandemics

3 Setup of a R&D pipeline for rapid development of antiviral compounds against emerging diseases

AVITHRAPID core expertises is based on 'Molecules development'

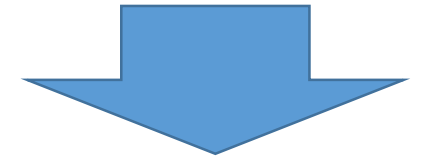
AVITHRAPID Consortium Composition

MAP OF EUROPE



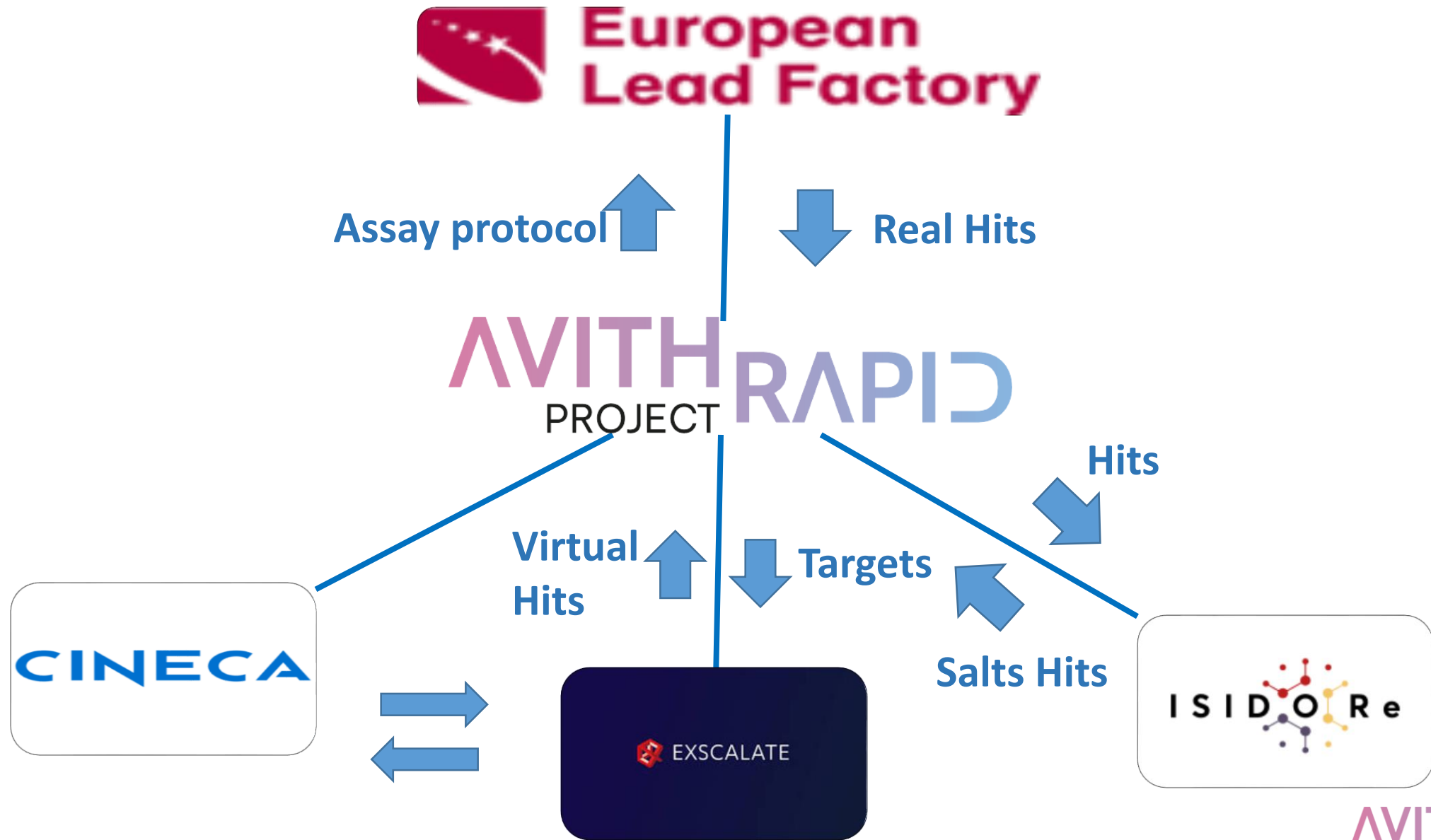
8 countries

Mainly universities
Two companies



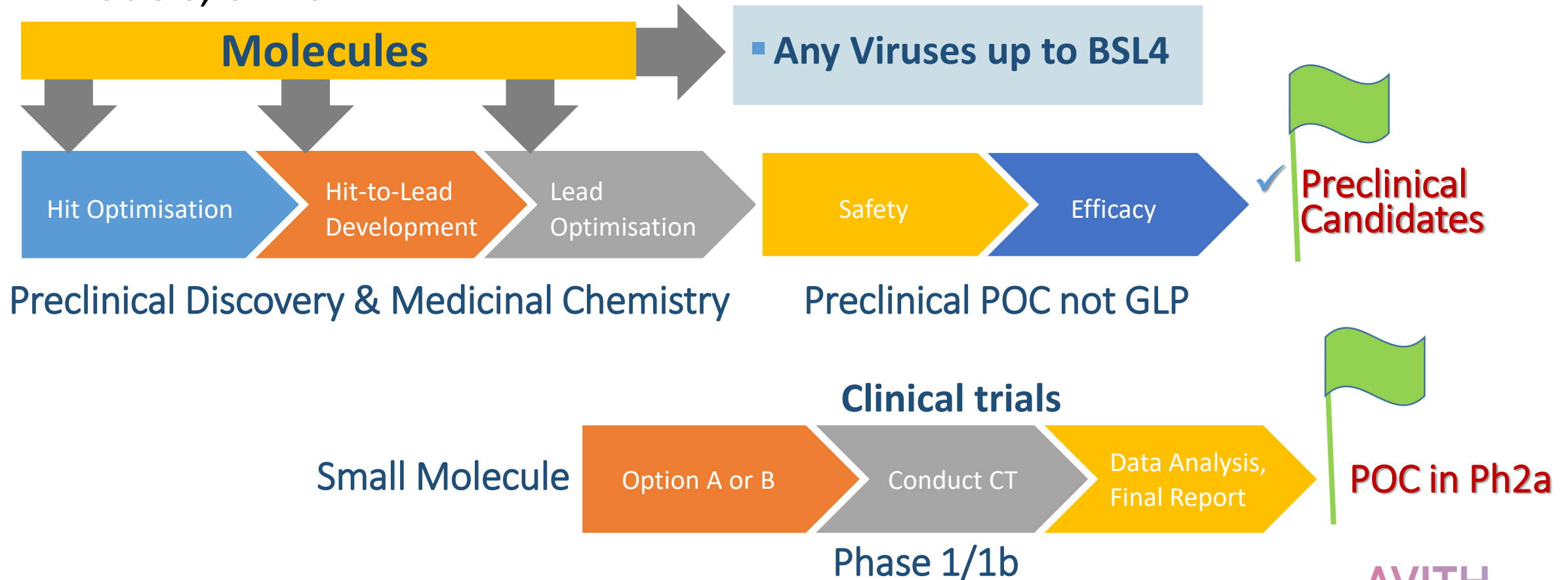
Open to collaborate
with other Consortiums,
Institutions, Companies
and Biotechs

AVITHRAPID example of collaborative networking

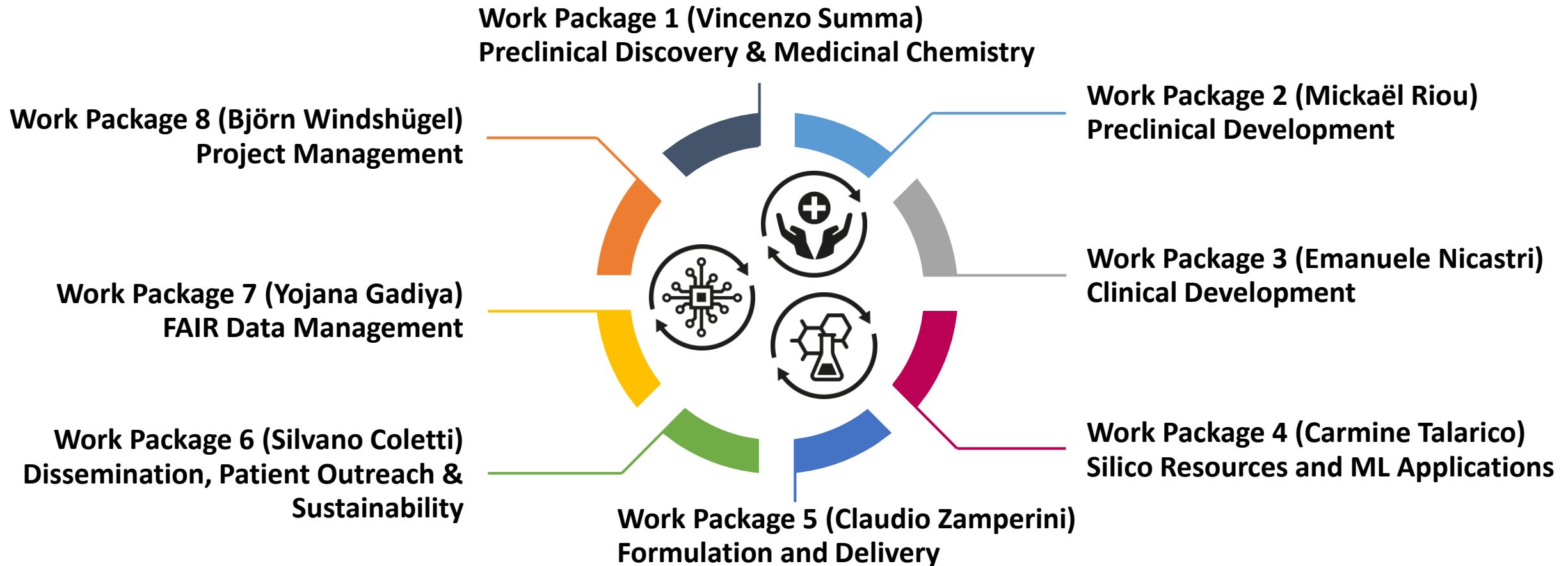


AVITHRAPID is an Early Development 'TEAM' (EDT)

- The Consortium is a multidisciplinary public-private Team
- Key expertises: viral biology, medicinal chemistry, structural biology, animal models, clinic

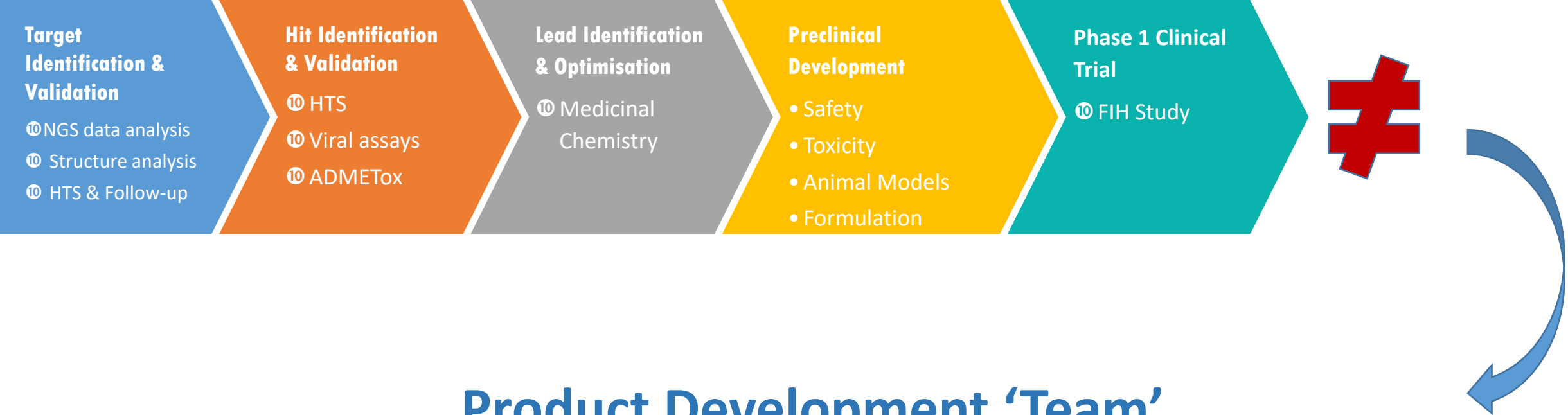


AVITHRAPID - EDT Work Packages organization



AVITHRAPID is an Early Development 'TEAM' (EDT)

EDT brings the agents to the POC in Human Ph1b/ Ph2a



Product Development 'Team'

Develops the agents coming from EDT in Ph 2/3 and approval

AVITHRAPID core expertise identification and development of 'Molecules'

'Our Molecules' based on synthetic capabilities

Small molecules

Conjugates to be linked to other small molecules or AB

Peptides/peptidomimetics/peptide conjugates

Nucleosides, nucleotides and prodrugs

'Our Assay' wet lab

Enzymatic assays up to 384 format- different read out - low to medium throughput

Antiviral & host Cell based assays BL2-BLS4 different read out - low throughput

Good viral 'collection' already available - the most relevant in house includes clinical isolates

260k molecules in house – 10k cmpds safe in man library for drug repurposing

In silico Screening

Ultra high performance -Exscalate

Structural biology

X-Ray & all physicochemical assays *in house*

AVITHRAPID consortium contribution to HERA Strategies

- *In silico* screening

- Enzymatic assays
- antiviral cell based assays up to BLS4
- counterscreenings

HPC

Assays

in vitro
in vivo

Molecules

- *In vitro- in vivo* ADME
- Animal model BLS3

- Med Chem
- Synthesis
- library 260k cmpds

All activities can be considered alone or in an integrated process

Consortium very flexible and proactive

AVITHRAPID needs / criticality

- GMP - GLP labs for API and regulatory tox to generate the IND package pre approval
- Only rodent animal models available in house
- CRO to support several critical activities
- Very large chemical library available for screening
- HTS with very large capacity
- A central system easily accessible, searchable and compatible to everybody
- Very strong dedicated infrastructure to carry on the activities (University labs)

What do we really need to be prepared for the next pandemic?

- Identify the key players in the antiviral field with proved track record
- **Create strong network between institutions to constitute stable, funded, monitored constantly 'centers of excellence' working on viruses**
- Promote constantly with public engagement the importance to work in antiinfectives
- Slim down the procedure to test agents in the clinic to achieve the efficacy POC

AVITHRAPID future plans

- Demonstrate to be an efficient 'Early Development Team'
- Increase the number of collaborations - network
- Be considered as possible partner for further initiatives in the antiviral projects
- Participate in the 'design' of new relevant initiatives for funding
- Increase activities in the Public Engagement



Thank You