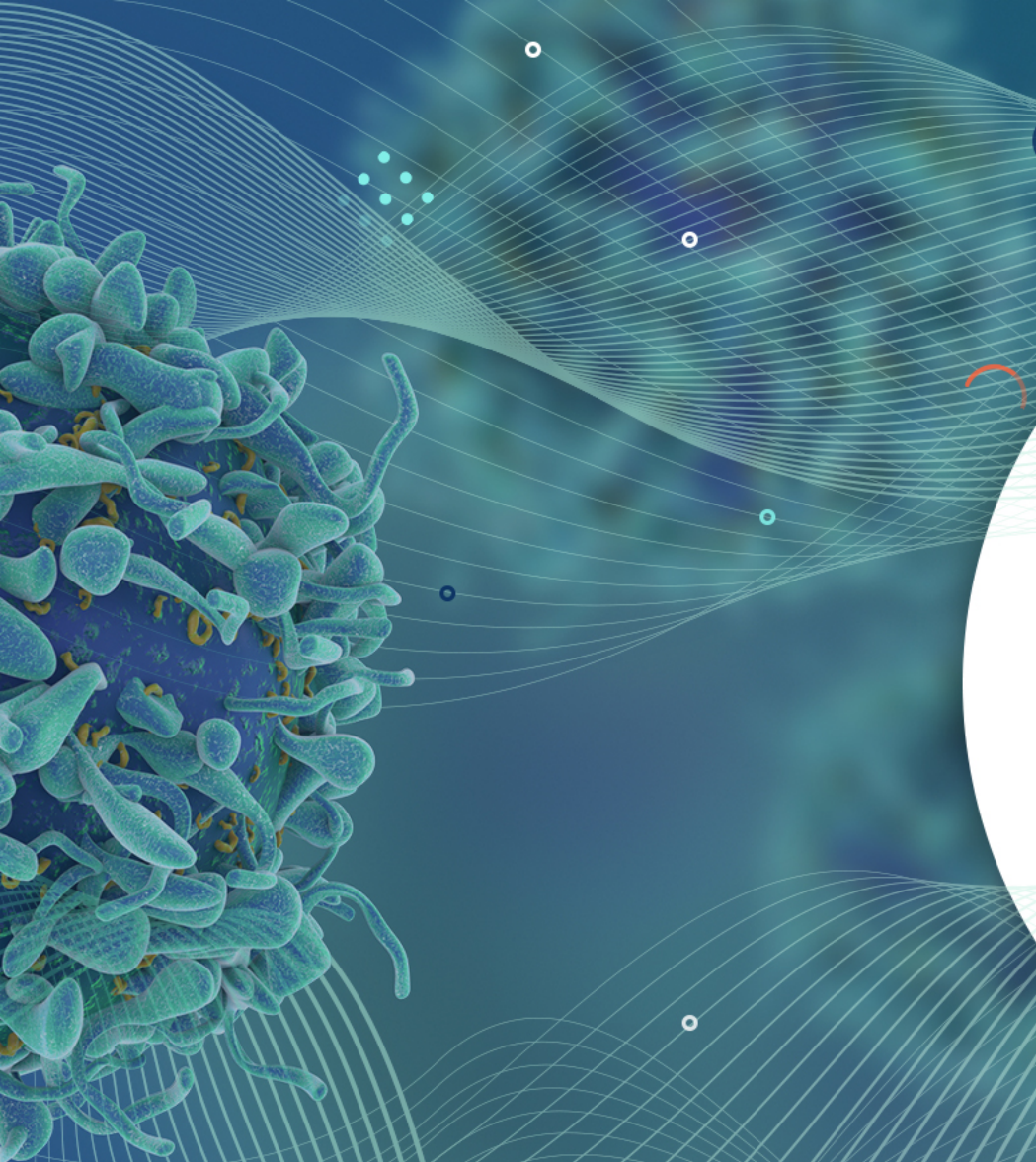


WEBINAR

HOW DO WE KEEP YOU IN THE RACE OF COVID-19 ?

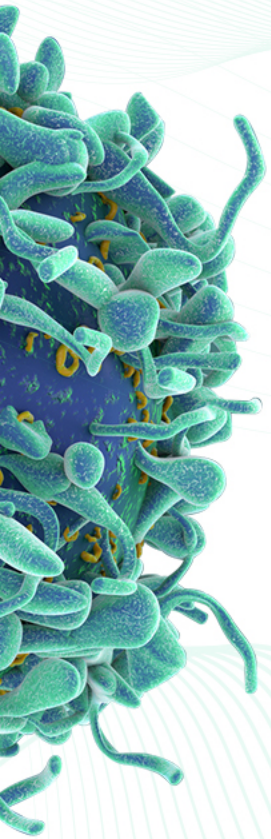
TOWARDS NEXT GENERATION SOLUTION PROVIDERS

October 16th, 2020

AFSSI Digital week

Oncodesign BIOTECHNOLOGY · cynbiose · Aepodia PARTNER IN EARLY PHASE® · PHARMALEX a.r.c. advanced regulatory consulting · ERBC THE NON-CLINICAL ENGINE

HOW DO WE KEEP YOU IN THE RACE OF COVID-19?



SUMMARY

I. The ongoing outbreak and the biopharma industry's answer

II. Challenges to overcome to find a solution against Covid-19?

III. How can we keep you in the race?
- Our alliance
- Spectrum of expertise

IV. Q&A session

TODAY'S SPEAKERS

Dr. Hugues COMTAMIN, DVM, PhD
Founder & CEO | Cynbiose | Cynbiose Respiratory

cynbiose

Xavier MORGE, Pharm. D., MBA
Chief Corporate Business Development Officer | Oncodesign

Oncodesign BIOTECHNOLOGY

Patrick Larcier, Pharm. D., MBA
Senior Director, Drug Development & Vigilance | PharmaLex France

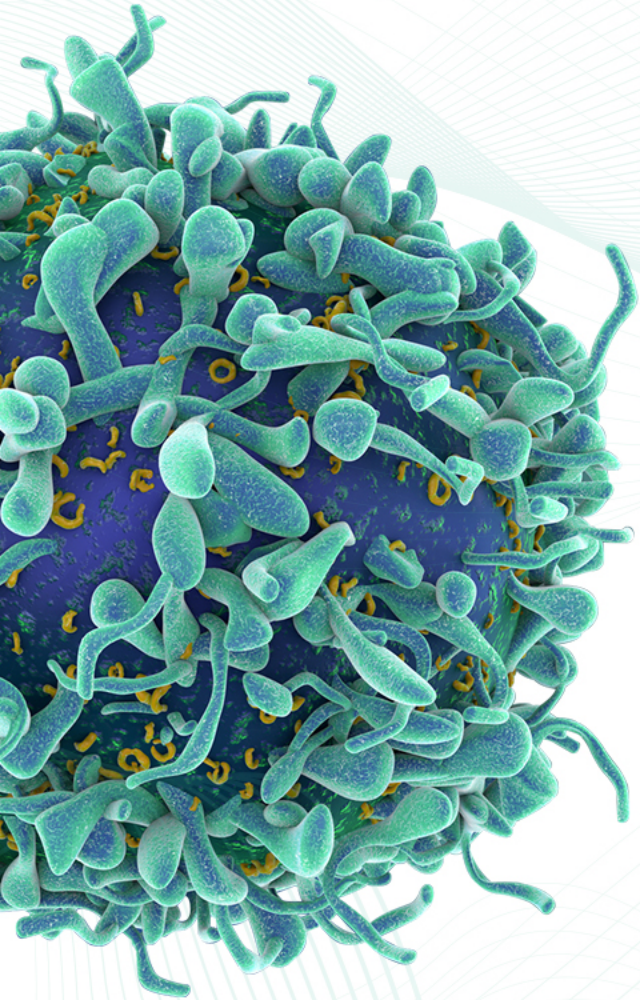
PHARMALEX

Marie-Laure SOLA, Pharm. D., ERT
France Client Service and Scientific expertise pole Director – ERBC

ERBC
THE NON-CLINICAL ENGINE

Denis GOSSEN
Co-founder | CSO | Aepodia

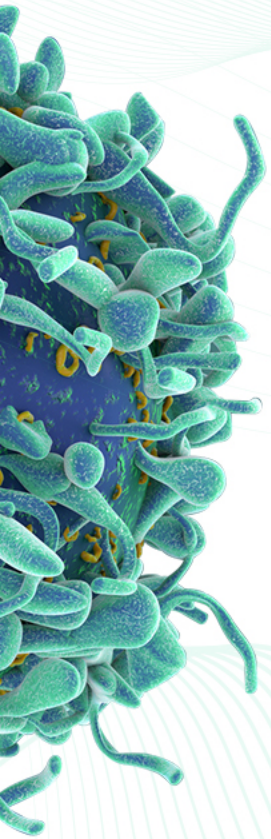
Aepodia
PARTNER IN EARLY PHASE®



The ongoing Covid-19 outbreak

Infectious diseases landscape

/ A state of constant vigilance

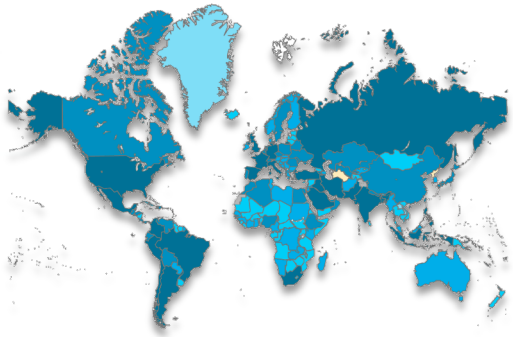


- For centuries, civilisations have had to deal with various epidemic outbreaks that often lasted several years:

- Viral zoonotic diseases & vector-borne diseases are considered as **major infectious risks** for the XXIst century => the players in the field of infectious disease research are in constant state of alert.

- Severe acute respiratory syndrome coronavirus 2 (**SARS-CoV-2**):

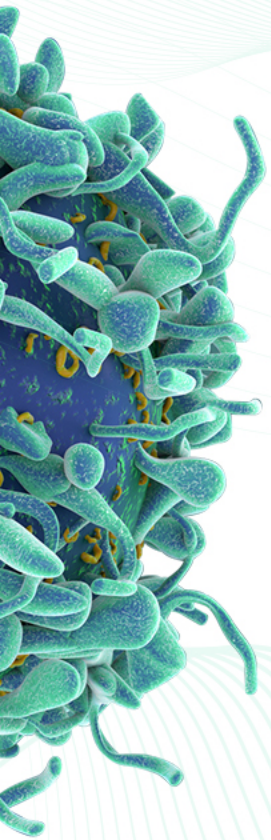
  > A respiratory virus
  > A new pathogenicity
  > Rapidly spreading, global impact



Source: WHO Coronavirus Disease (COVID-19) dashboard, October 6th, 2020

Biopharma industry's answer to COVID-19 outbreak

/ The race against time



$$

INVESTMENTS IN DRUG DEVELOPMENT

> 15-20 billion US$

SPEED-to-MARKET

> Repurposing of products (40%)

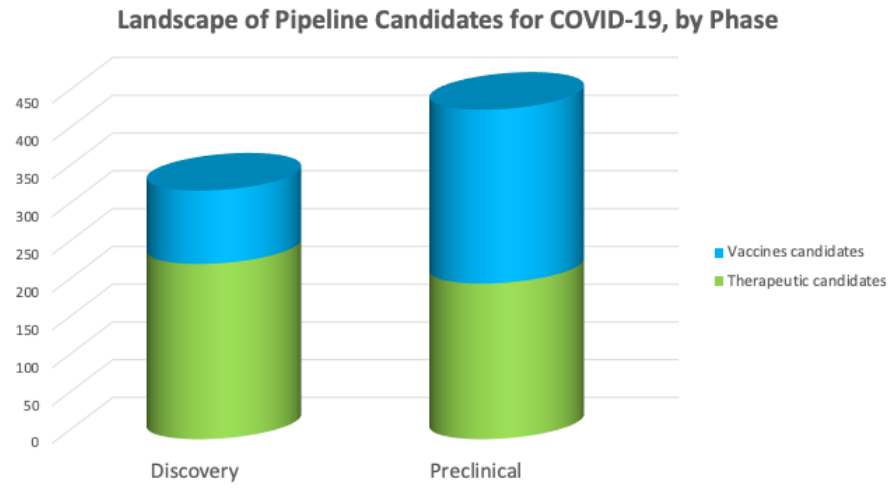
> 400 on-going clinical trials

A CROWDED PIPELINE

> 1 200 therapeutics and vaccines in the global pipeline

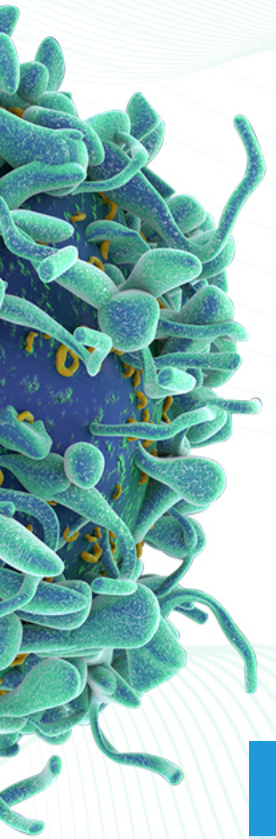
> Early non-clinical pipeline

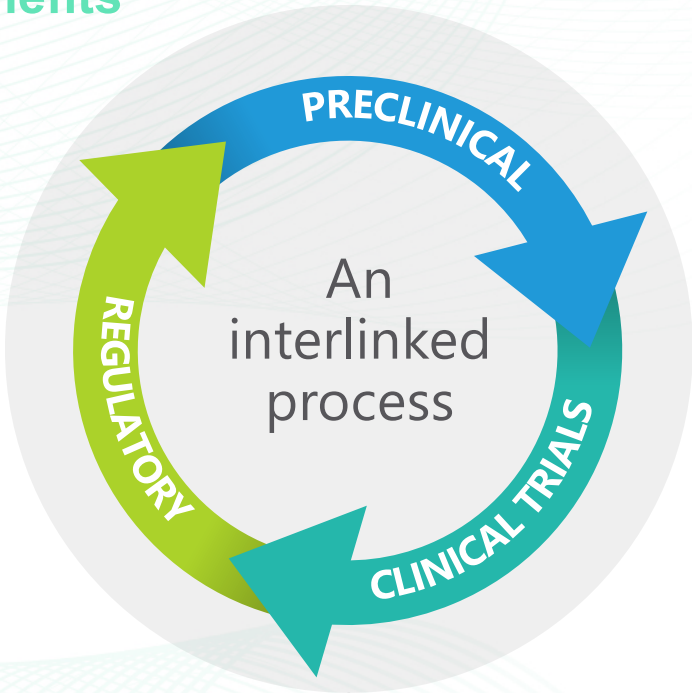
- **51 % innovative candidates**
- **Biologics** incl Vaccines (84%) **vs Small molecules** (16%)



Biopharma's agility to face the COVID-19 outbreak

/ Be smart for humankind benefits





PRECLINICAL

> Effective and **predictive *in vitro*** assays & ***in vivo*** models

> Importance of **translational** preclinical research

CLINICAL TRIALS

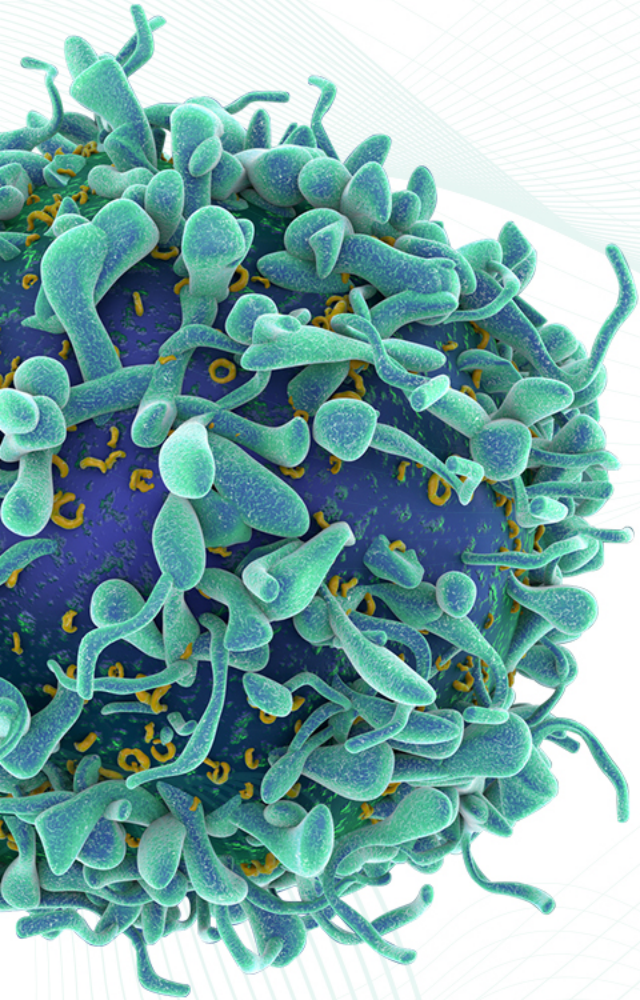
> Safety

> Recruitment of patients

REGULATORY

> Therapeutic vs medical device

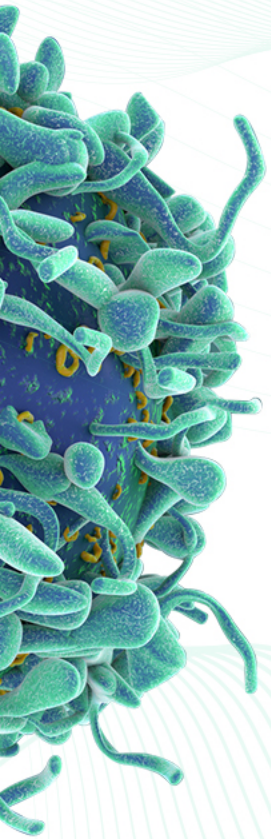
> Existing regulatory landscape: development steps and filings



Challenges to overcome to find a solution against Covid-19

Regulatory challenges

/ How to optimize regulatory steps?

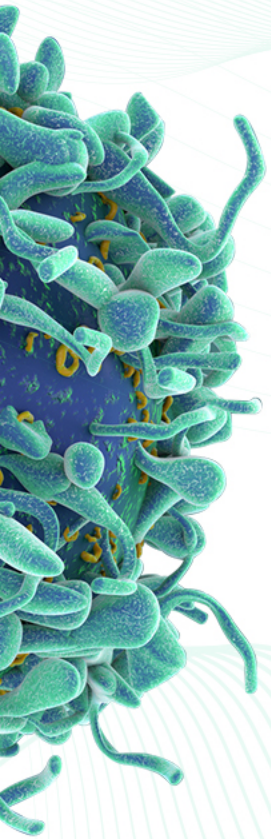


Description	European Union	United States of America
Serious cond. / unmet need	(Rolling Review)	Fast Track
Expedite development	PRIME	Breakthrough Therapy
Surrogate endpoint, unmet need	Adaptive Pathways	Accelerated Approval
Shorter licensure assessment	Accelerated Assessment	Priority Review (PR)
Unlicensed / Investigational		Emergency Use Authorization
Efficacy data not available **YET**	Conditional MA	
Efficacy data **NOT** foreseen	Ma IN Exceptional Circumstances	Animal Efficacy Rule

Use of existing tools for development as well as MAA/BLA in the two main regions

Regulatory challenges: examples

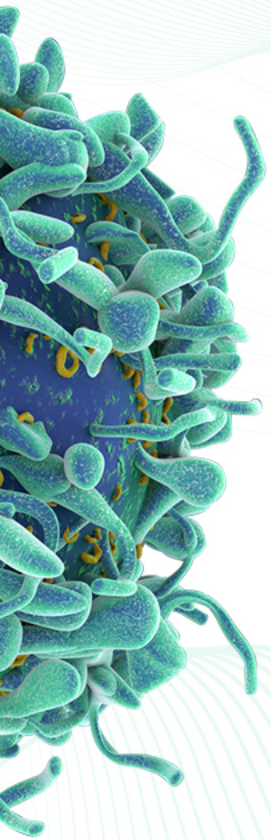
/ How to optimize regulatory steps?



Name, description	European Union	United States of America
Remdesivir	**Conditional** MA 2020-Jun	**EUA** 2020-May
Smallpox treatment TPOXX (tecovirimat)		Fast Track, **Animal rule**, **PR Voucher** 2018-Jul
Smallpox/monkeypox vaccine (MVA-BN)	MA in **Exceptional** Circumstances 2013	Fast Track, **Pre-EUA**, **PR Voucher** 2019-Sept
Ebola vaccine (Ervebo, Merck, 1 dose)	PRIME, Accelerated assessment **Conditional MA** 2019-Dec	Breakthrough therapy, **PR Voucher** 2019-Dec
Ebola vaccine (Janssen, prime-boost)	Accelerated assessment, **MA in Exceptional Circumstances** 2020-Jul	**?**

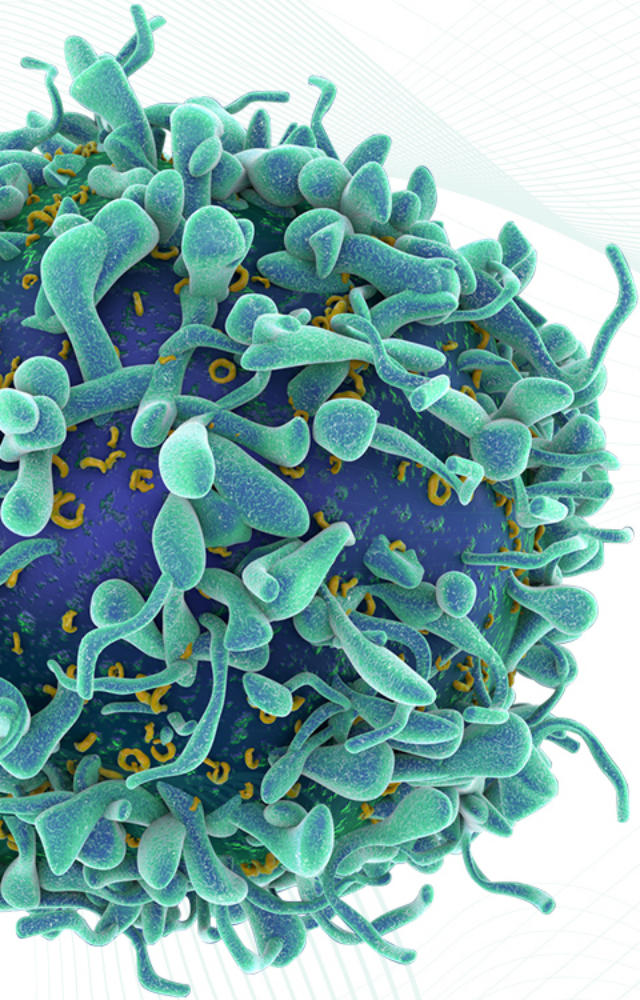
The importance of a valuable preclinical and early clinical package

/ Support and influence clinical strategies



- Repurposing drug candidates
- Prophylactic and Therapeutic vaccine candidates
- Fit-for-purpose models
- Regulatory assessments

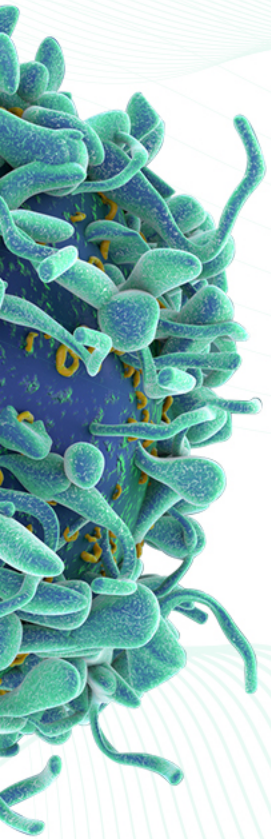
Biopharmas companies benefit from our innovative service solutions to accelerate entry into clinics and their market access.



How can we keep you in the Covid-19 race?

Our original alliance

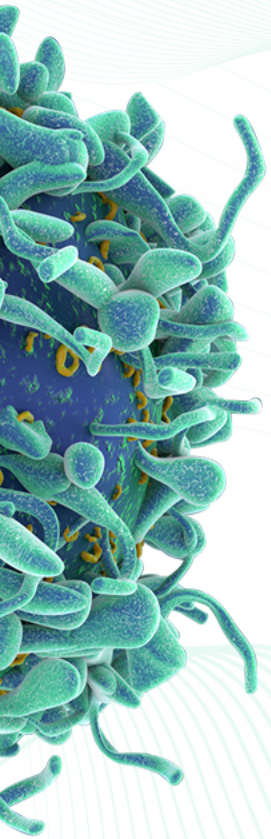
/ Network of partners



- **Oncodesign, Aepodia, ERBC, Cynbiose & PharmaLex**: a network of partners convinced that fast and complex drug developments require the use of a collaborative & creative research organization network
- We bring together:
  - Thorough understanding of drug development challenges
  - A comprehensive view of the drug development process
  - State of the art & cutting-edge approaches
  - Technological platforms
  - Ability to set up an appropriate project governance structure
  - End-to-end solutions

Our original alliance

/ Network assets & values



Fit-to-purpose solutions

- Fully integrated preclinical drug discovery services
- Preclinical & clinical drug development
- Comprehensive technological preclinical & clinical expertise
- Regulatory & development Strategy

Predictive and translational research capabilities

- Broad range of valuable preclinical models and assays
- Technological platforms at the forefront to support multidisciplinary & scientific teams

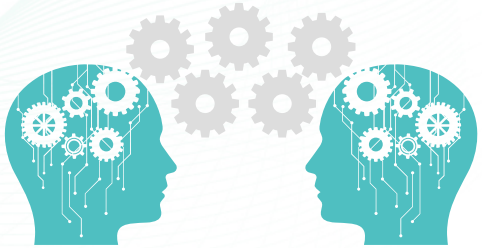
Extended & selected network of clinicians, academics and industrial partners

Client-driven & flexible organization

- Dedicated & responsive project manager
- Alliance partnership agreement
- Integrity, agility, solidarity

A continuum of specialties to unlock the scientific padlocks linked to Covid-19.

Spectrum of expertise



DISCOVERY

PRECLINICAL STUDIES
Exploratory studies GLP studies

IND/CTA

CLINICAL STUDIES

Oncodesign BIOTECHNOLOGY — From Discovery to IND/CTA for innovative therapies thanks to precision medecine

cynbiose — Exploratory pharmacology, safety & PoC studies in translational non-human primate models

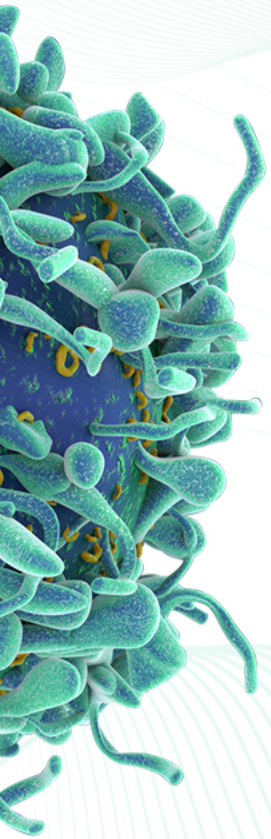
ERBC THE NON-CLINICAL ENGINE — Advice & complete on a timely manner preclinical pharmacology and regulatory studies

Aepodia PARTNER IN EARLY PHASE® — Design & manage early clinical studies

PHARMALEX a.r.c. advanced regulatory consulting — Regulatory & pharmacovigilance

Oncodesign

/ Committed to help finding innovative treatments against pandemic COVID-19 disease



Fit-to-purpose solutions

- Biochemical assays
- Cell assays
- Animal disease models
- Immunomonitoring & viral loads in clinics

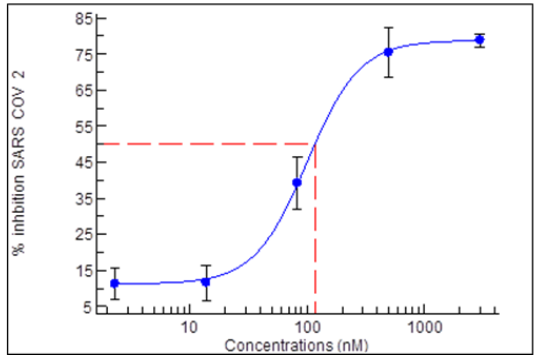
In vitro assays

- Compound binding to spike or ACE
- Spike S – ACE, protein-protein interaction
- TMPRSS2, protease enzymatic assay

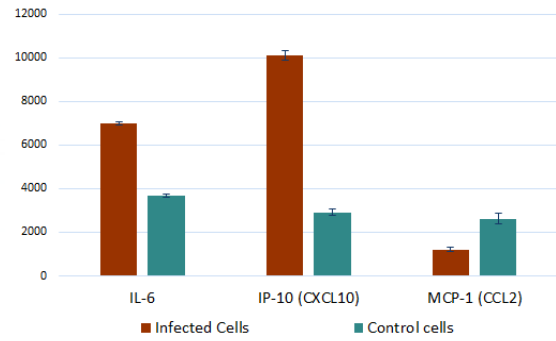
Cell assays

- Human lung epithelial cells
- Viral load
- Cytopathogenic effect
- Immune modulation

Inhibition of SARS-CoV2 infection in VeroE6-TMPRSS2 cells by the PIKfyve inhibitor Apilimod

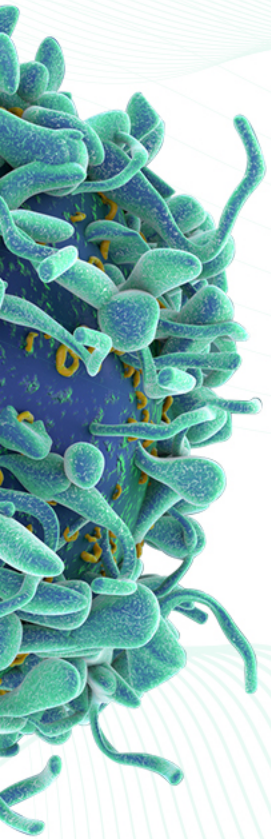


SARS-CoV-2-induced cytokine in Calu-3 cells (multiplex bead assay)



Oncodesign

/ Committed to help finding innovative treatments against pandemic COVID-19 disease



Animal disease models

- SARS-CoV-2 infected animal models
  - Gloden Syrian
  - Cynomolgus macaque
- Pulmonary fibrosis

- Clinical monitoring & scoring
- Viral load
- Organ histology
- Cytokine profiling (qRT-PCR, ELISA)
- Immune cell phenotyping (FACS)
- Antibody response (ELISA, neutralization)
- DMPK/PD
- Non-invasive nuclear imaging (Macaque)

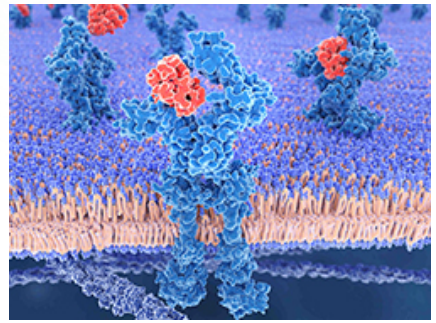
Clinical trial

- Cytokine storm
- Viral load

Acute Respiratory Distress Syndrome (ARDS)

Client-driven & flexible organization

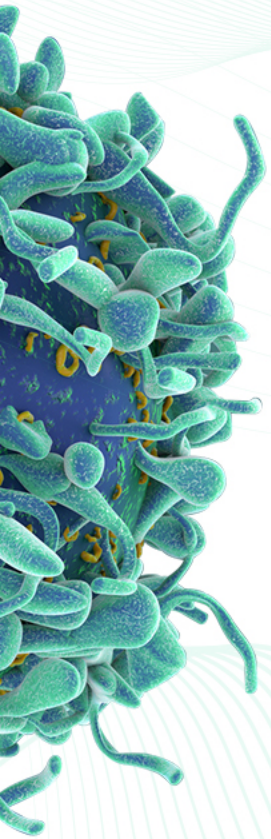
- New model to become
- Dedicated & responsive project manager
- Alliance partnership agreement
- Integrity, agility, solidarity



Cytokine Storm

Cynbiose

/ Derisk your lead in a translational preclinical model



Fit-to-purpose translational solutions for infectious & respiratory diseases

- **NHP *in vivo* model**, relevant for assessing immunotherapies and vaccines in these therapeutic areas
- Extensive expertise and capabilities in **infectious diseases**
- **Exploratory** pharmacology, immunogenicity and early tox (pulmonary, …)
- Unique capabilities for **aerosol therapies**

Cell line

Reconstituted human airway epithelium models of SARS-CoV-2 infection

PK / PD

Immunogenicity

Early tox, Immunotox

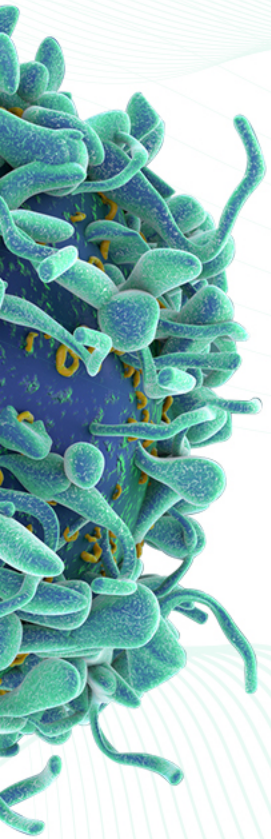
SARS-CoV-2 NHP model:

- human strain
- routes of admin (IN, IT, aerosol, …)
- samplings
- virological analysis

A full package of preclinical services

Cynbiose

/ Derisk your lead in a translational preclinical model



State-of-the-art facilities and quality

- Animal facility: AAALAC accredited, BSL-2/3, GMOs
- Ethics & animal welfare: a major concern
- QMS: GLP-like

Cynbiome®

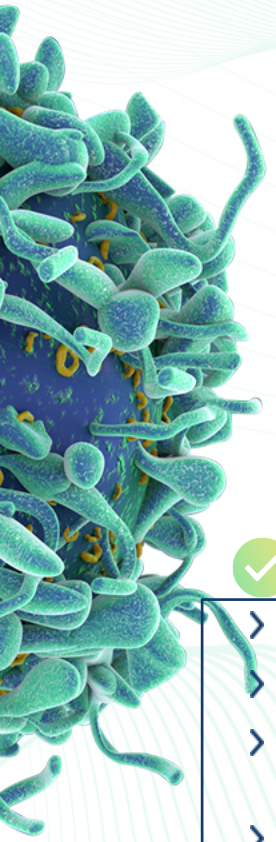
- A new area of preclinical research on the relationship between **microbiome and infectious diseases**
- 1st **preclinical network of excellence** with French partners (biopharmas, CROs and academic teams)

Client-driven & flexible preclinical CRO

- **Flexibility, agility**, advice
- Design of customized and flexible **protocols**
- Extended & selected **network** of scientific partners
- **Strong customer relationship** and support

ERBC

/ What preclinical studies before First In Man?



Follow the appropriate guideline

- ISO for medical device, ICH M3 R2 for NCE, ICH S6 for biologics, WHO for vaccine, EMEA guidelines
- GLP environnement

Adapt the experimental plan

- Mimic what will be done in clinical use: route and administration schema
- Chose the species (rodents rat or mouse and/or non rodent dogs, NHP, minipigs, rabbits)
- Define the duration based on the intented clinical duration
- Chose the relevant biomarkers

Example: New Chemical Entity

- Analytical validation for formulation and bioanalysis
- Genotoxicity
- Repeated toxicology in **2 species** rodents and non rodents, including TK evaluation
- Safety pharmacology, core battery: CNS, respiratory, cardiovascular (non rodent telemetry and in vitro hERG)

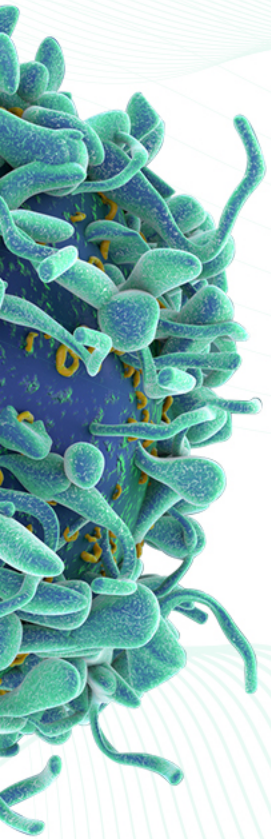
Example: vaccine

- Analytical methods (Ab levels by ELISA,cellular immunity by ELISPOT)
- Repeated toxicity studies in **a single species** who should develop an immune response, susceptible to the pathogen, including local tolerance. Same number of injections as intented in Humans but with 2-3 weeks between 2 injections
- Biomarkers: cytokines, CRP
- Safety pharmacology: included in tox study or stand alone studies

Case by case approach: repositionning based on data already available (bridging study), biologics, ATMP

Aepodia

/ First-in-Man up to Proof-of-Concept Clinical Trials



Review and Advice on Preclinical-Clinical Package

- Mechanism of action (MOA) and potential biomarkers of activity
- Clinical Development Plan including disease biomarkers, translational medicine
- Preclinical Development including Regulatory package to support FIM
- Regulatory Submissions (CTA) and Scientific Advice

Operational Excellence – GCLP/GCP Environment

- Clinical Project Managers experienced in early clinical trials with multiple partners
- Ongoing review of generated data – permanent adjustment – proactivity / anticipation

Extended & Selected Network of Clinicians, Academics Hospitals and Industrial Partners

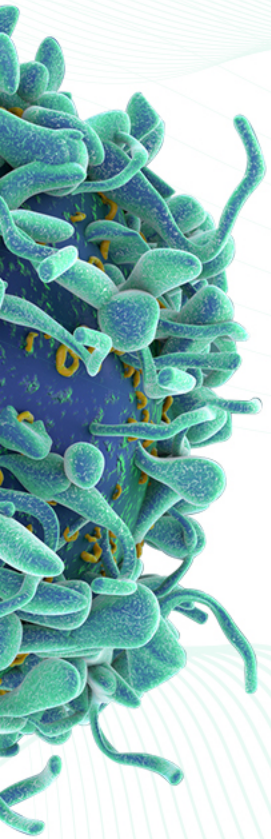
- All experienced in Phase I-II clinical trials (e.g. multiple amendments)

Client-Driven & Flexible Organization

- Dedicated & responsive project manager
- Alliance partnership agreement
- Integrity, agility, solidarity

Aepodia

/ Clinical Trials during COVID-19 Pandemic Situation (non exhaustive list !)



Trial Management & Monitoring

- Training for Data Integrity & Data Privacy for Home Nurses – access to Source Data and SDV – remote monitoring
- Clinical Trial Materials – direct supply to patients at home – adjust visit of nurses at home
- Vendors – Central laboratories – Suppliers (ALL !)
- Import/Export of biological samples (custom clearance)
- Risk Management Plan

Data Management

- eCRF completion Guidelines in case of positive testing to Sars-CoV-2– MedDRA coding & conventions – data base checks
- Enable Snapshot of Clinical database – “permanent” or at least regularly – reporting tools – medical review

Informed Consent, Protocol and Clinical Stud Report

- Adjust Informed Consent - Manage Protocol Deviation in a timely manner – impact on study – Substantial Amendment – Urgent Safety Measures – Temporary Halt

Trial Master File (TMF) – temporary halt for paper collection / organize scanning

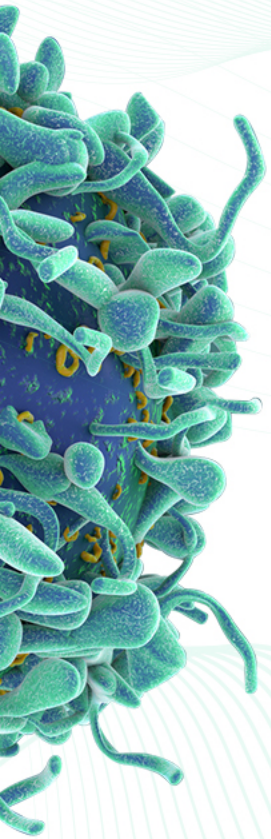
Guidance to Clinical Sites and Patients !

Ref: Guidance on the management of clinical trials during COVID-19 pandemic: https://ec.europa.eu/health/documents/eudralex/vol-10_en

PharmaLex

/ Confidence beyond Compliance

PHARMALEX
a.r.c. advanced regulatory consulting



Fit-to-purpose solutions

- CMC (Quality), Preclinical & Clinical drug development
- Regulatory & Development Strategy
- Data Management & Statistics
- Medical writing services (IMPD/IND/IB and CSRs)
- Ad-hoc development and Regulatory Consultancy
- Regulatory and PharmacoVigilance Surveillance

Extended & selected network of experts and company partners

Client-driven & flexible organization

- Dedicated & responsive project manager
- Alliance partnership agreement
- Integrity, agility, solidarity

Spectrum of expertise

DISCOVERY

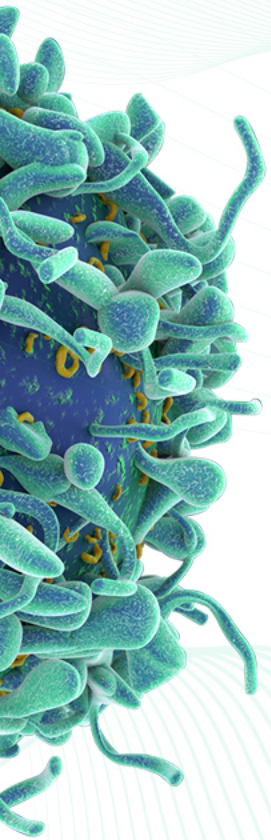
PRECLINICAL STUDIES

Exploratory studies | GLP studies

IND/CTA

CLINICAL STUDIES

Oncodesign Biotechnology	From Discove	In vitro assays / Animal disease models Immunomonitoring / viral load pharmaco-imaging / PK/PD	Immunomonitoring / viral load pharmaco-imaging / PK/PD
cynbiose	Exploratory pharma … dies in translational non-H	Pharmacology & Safety studies: PK, PD, Immunogenicity, Immunotox, PoC studies (incl. Infectious) Biomarkers / Imaging, Microbiome	Efficacy studies (infectious & respiratory, SARS-CoV-2) Immunopharmacology Physiological barriers crossing studies Biomarkers / Imaging
ERBC The Non-Clinical Engine	Advice … m	Preliminary non GLP toxicity MTD/DRF (rodent / non-rodent) Pharmacology models	Toxicology *(incl. TK, immunomonitoring):* single / repeated dose - GLP Case by case depending on the test item *(GLP)*: › Safety pharmacology › Reproductive & developmental toxicity *(fertility, Embryo-foetal)* › Genotoxicity
Aepodia Partner in Early Phase®	Design &	Biomarker / pharmaco-imaging	From First in Man to Clinical PoC Biomarkers & PK / PD
PHARMALEX a.r.c. advanced regulatory consulting	Development strategy & regulatory development advices		



Question & Answer Session

your Innovative Solution Providers

from Discovery to First-in-Man requests

Oncodesign® BIOTECHNOLOGY

cynbiose

Aepodia PARTNER IN EARLY PHASE®

PHARMALEX a.r.c. advanced regulatory consulting

ERBC THE NON-CLINICAL ENGINE

CONTACT US

Come along to question your new Innovative Solution Providers from Discovery to First-in-Man requests.

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