



*Fondazione per la Ricerca  
sulla Fibrosi Cistica - ETS*  
italian cystic fibrosis research foundation

**WEBINAR DI  
PRESENTAZIONE**  
15-17 GENNAIO 2024





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**Alessandra Bragonzi, PhD**

Infections and Cystic Fibrosis Unit &  
Cystic Fibrosis animal Core Facility  
Division of of Immunology, Transplantation and Infectious Diseases  
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**WHAT**

Accelerating innovative treatment strategies for Cystic Fibrosis through pre-clinical research

**WHY**

Provide infrastructure (stability and BSL2/3) and expertise in CF animal models; reduce individual center costs associated with maintaining CF colonies research

**WHO**

Myself and collaborators (Ida De Fino, Alice Rossi, and Davide Gugliandolo) with unique expertise in maintaining CF colonies and modeling respiratory infectious diseases

**WHERE**

Operating in Milan at OSR (Ospedale San Raffaele) with the financial support of FFC colonies

**WHEN**

Ongoing initiative since 2009

## Level 1

- Distribution of CF mice ready to be used



## Level 2

- Scientific and regulatory support to plan preclinical studies
- Pre-clinical models of respiratory infection
- Pharmacological treatments



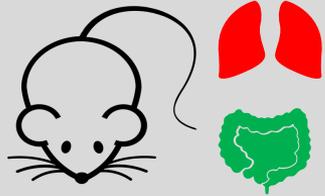
## Level 3

- Activities described at Level 1
- Processing and analysis of biological samples
- Data analysis including statistical and scientific report



# Cystic Fibrosis Mouse Models

**C57BL/6 *Cftr* tm1<sup>Unc</sup> TgN(FABPCFTR)** (Snouwaert, 1992; Zhou, 1994)



CFTR knock-out gut corrected

C57BL/6J *Cftr* exon 10 replacement (S489X)/ FABPhCFTR insertion

Lung phenotype: abnormal nasal potential difference, inflammatory response, infection clearance; Gut phenotype: normal; Alimentary phenotype: normal; Lethality-postnatal: normal



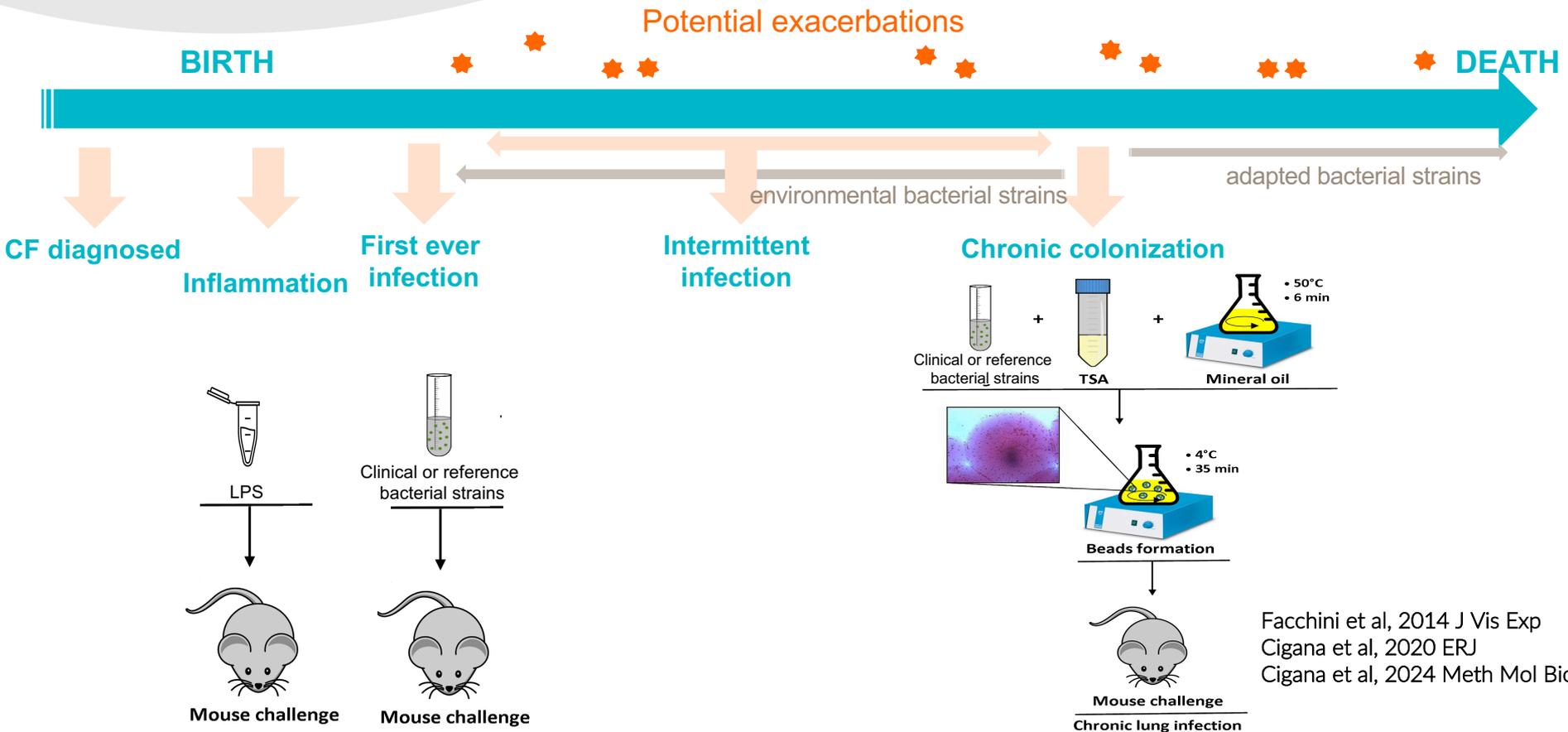
**C57Bl/6 *Cftr*<sup>Δtm1Kth</sup>** (Zheier et al, 1995)

CFTR deltaF508

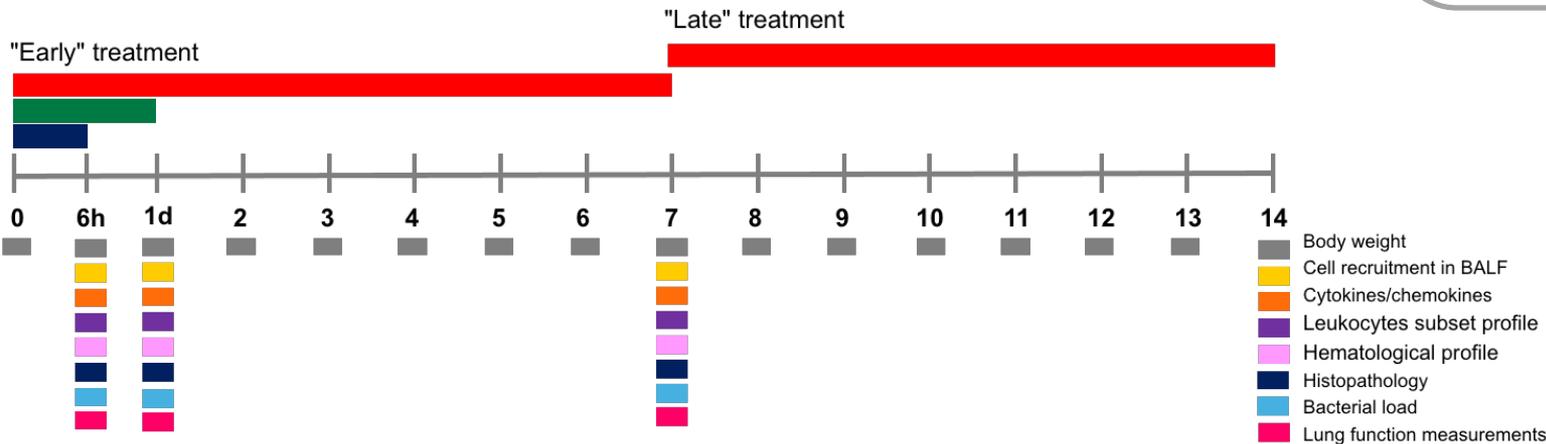
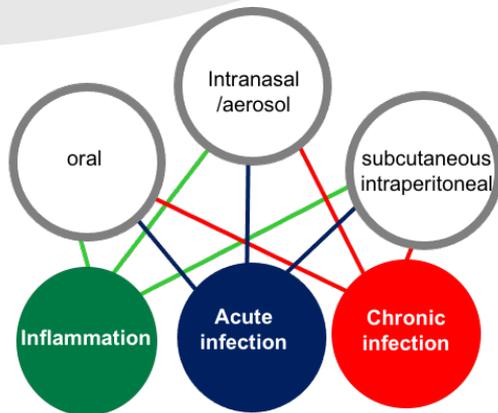
C57BL/6J *Cftr* delta F508 with 3 bp deletion in exon 11

Gut phenotype: obstruction; Lung phenotype: abnormal nasal potential difference, inflammatory response, infection clearance; Alimentary phenotype: normal + laxative; Postnatal lethality: high mortality pre and post-weaning

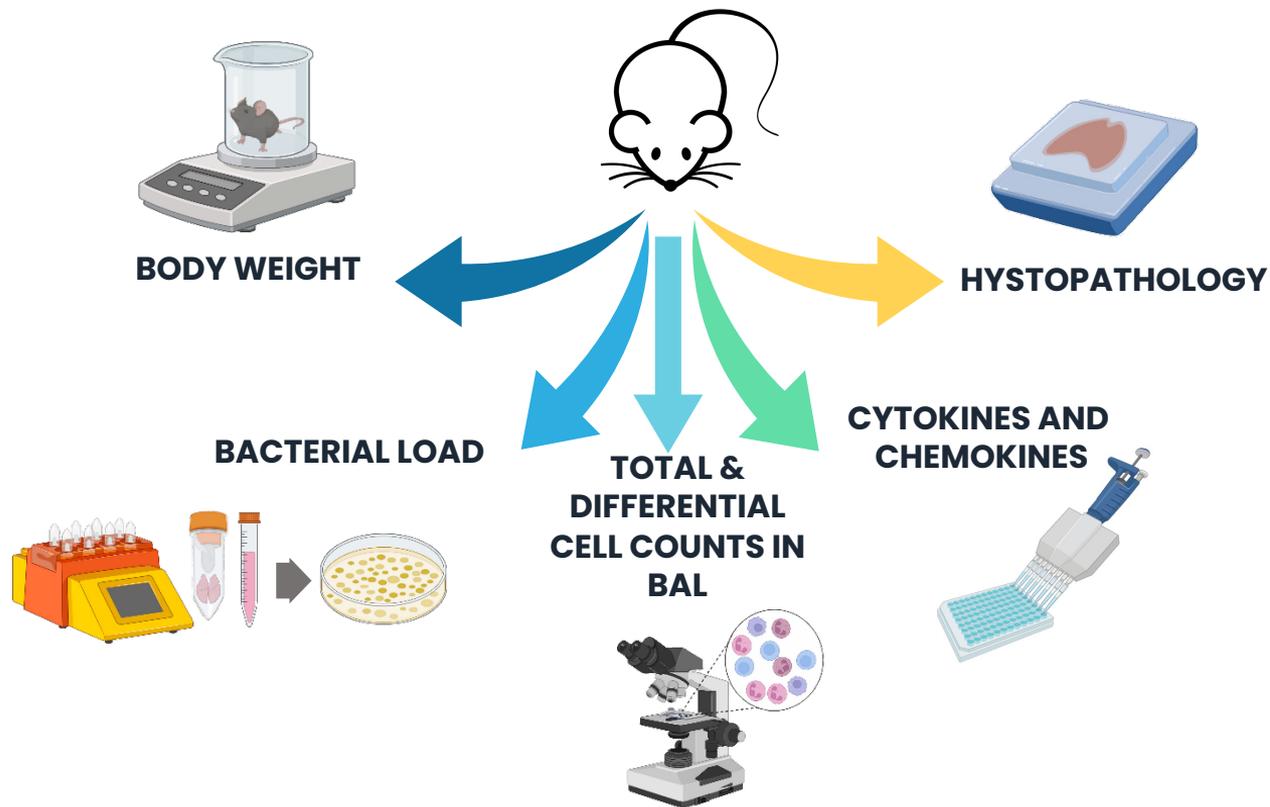
# Pre-clinical Efficacy Mouse Model



# Schedule of treatment and read-out



# Traditional and extended read-out



## FLEXIVENT LUNG FUNCTION MEASUREMENT



PARAMETER	DESCRIPTION	PHYSIOLOGICAL RELEVANCE
FEV <sub>x</sub>	Forced Expiration Volume data	Amount of air forcefully exhaled (drawn) at different time points
FVC	Forced Vital Capacity	Amount of air the animal can physically exhale
R <sub>rs</sub>	Resistance of the respiratory system	Airway constriction
E <sub>rs</sub>	Elastance of the respiratory system	Stiffness
C <sub>rs</sub>	Compliance of the respiratory system	Ability to stretch



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# Additional Support Services

**Francesca Sanvito**  
Pathological Anatomy Unit  
Ospedale San Raffaele

## TOXICITY STUDIES

Toxicology; Necropsy and tissues collection managed by computerized system (Ascentos)



## PATHOLOGICAL STUDIES

Histological preparation; Special staining; Immuno histochemistry; Histopathological evaluation; Reporting managed by computerized system (Ascentos)

**Micol Ravà**  
Animal Biochemistry  
Ospedale San Raffaele

## HEMATOLOGY

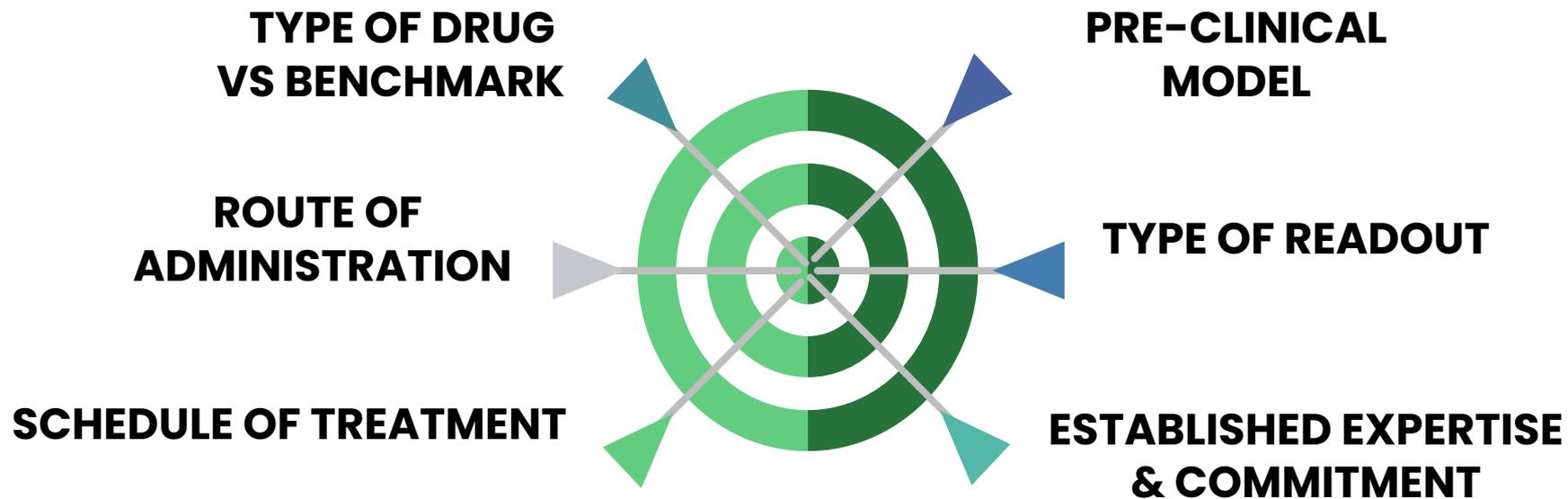
Complete Blood count (WBC, WBC count, RBC, HGB, HCT, MCV, MCH, MCHC, PLT, and reticulocytes by Idexx Procyte analyzers)

## CLINICAL BIOCHEMISTRY

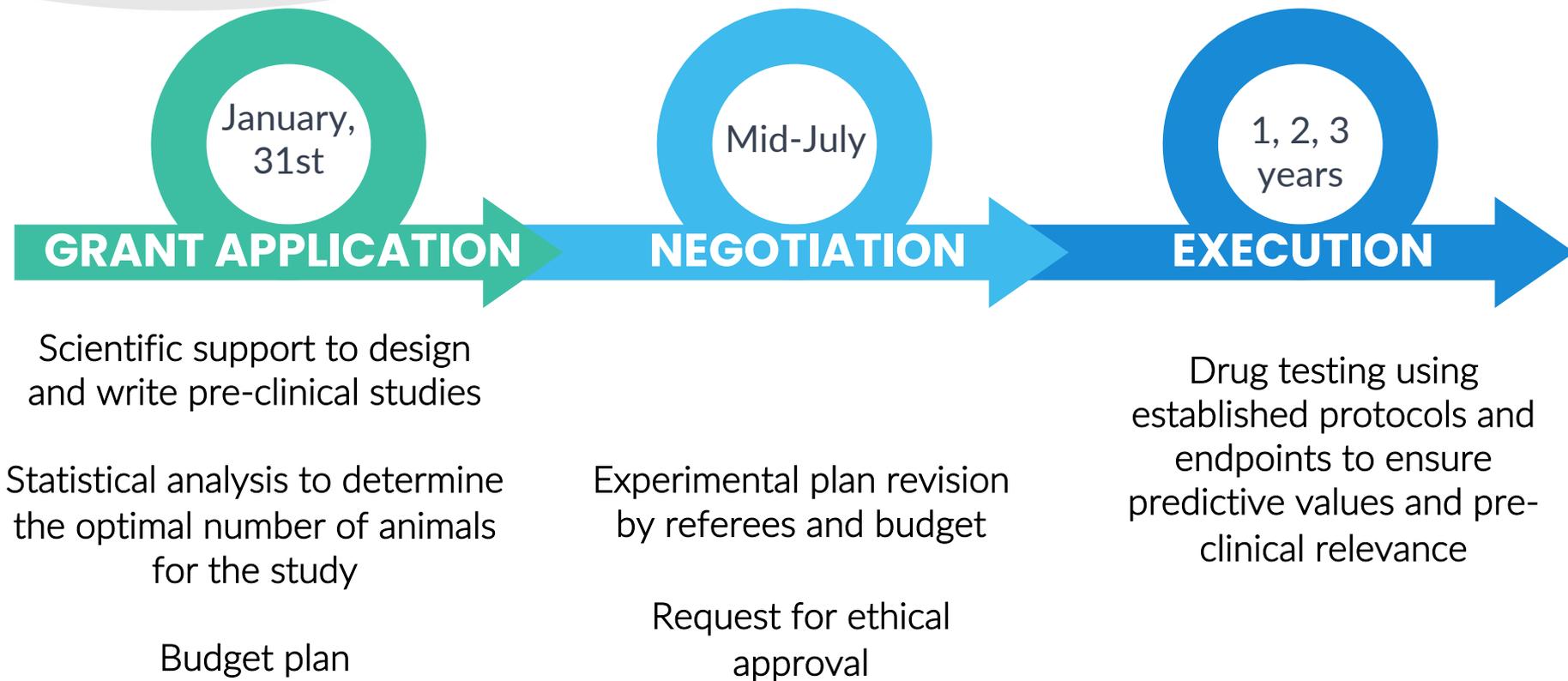
21 parameters of serum biochemical tests for liver, kidney, heart, pancreas and other



# Critical Success Factors for Effective Drug Evaluation



# How to Access the Service



## CF mice

Wild type: 100% project charge (20 €)  
CF KO mice : 50% project charge (103 €) and 50%  
founded by CFaCore (103 €)

Payment  
to FFC

## Charles River mice

C57Bl/6: 100% project charge (20 €)  
Animal delivery: 100% project charge

Payment  
to Charles River

## Services

BSL2 stabulary: 100% project charge  
Consumable: 100% project charge  
Personnel: 0% project charge, founded by CFaCore

Payment  
after OSR  
invoice



**Alessandra Bragonzi**

26 years of experience in CF.  
Since 2009,  
founder and head of  
CFaCore



**Ida De Fino**

20 years of experience in CF.  
Since 2010, responsible for  
the management of  
transgenic CF mice



**Alice Rossi**

14 years of experience in animal  
models and 11 years in CF.  
Since 2013, responsible for the  
pre-clinical studies



**Davide Gugliandolo**

5 years of experience in animal  
models and 3 years in CF.  
Since 2021, responsible for  
animal care and assisting pre-  
clinical studies

**Our achievements:** 55 projects for efficacy testing studies  
46 projects for CF mice; 79 publications on mouse models of CF



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