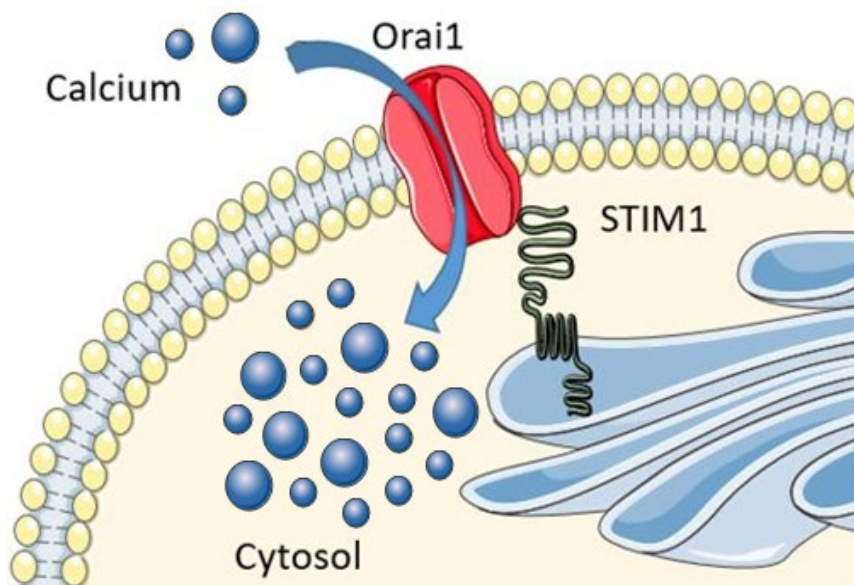




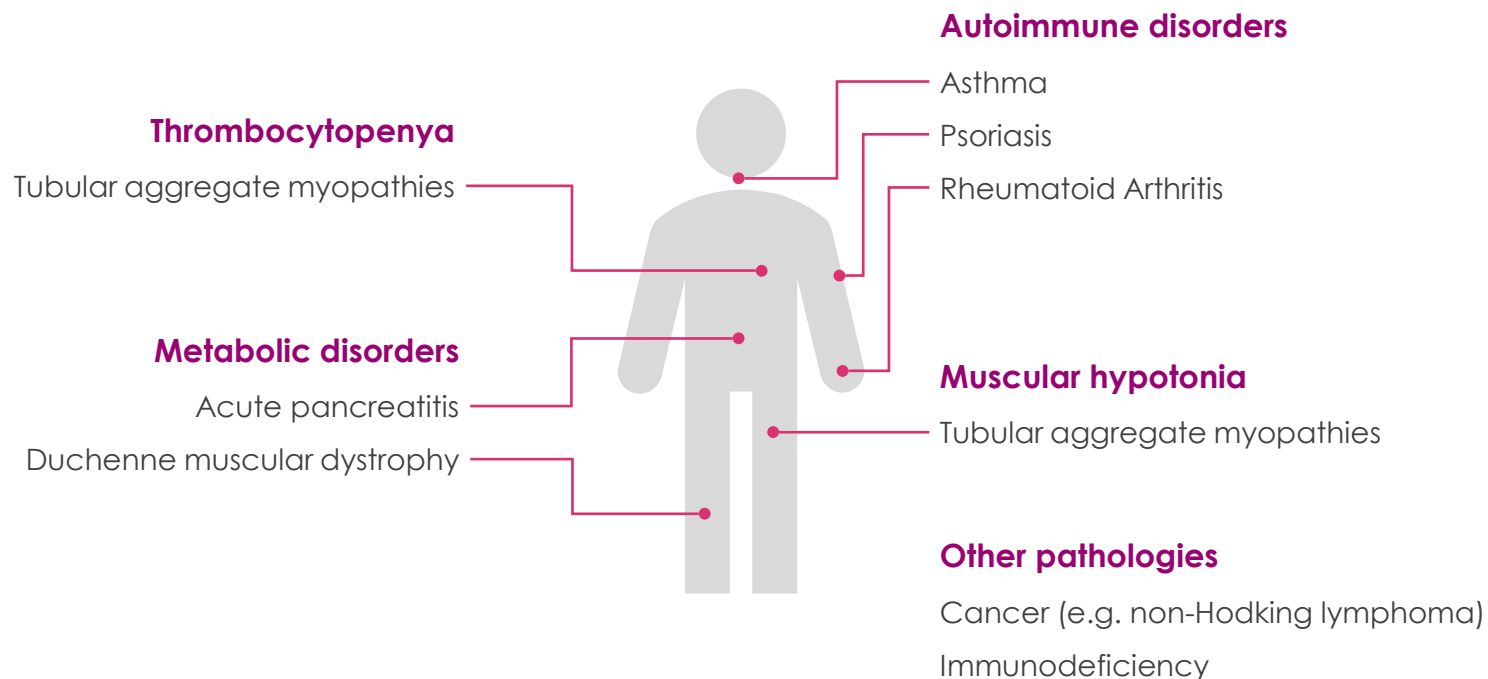
**Chemi@re<sup>++</sup>**  
It's a rare thing to care

## SOCE over-activation



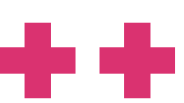
- Important mechanism in the  $\text{Ca}^{2+}$  homeostasis maintenance

## Transversal mechanism in many disease contexts

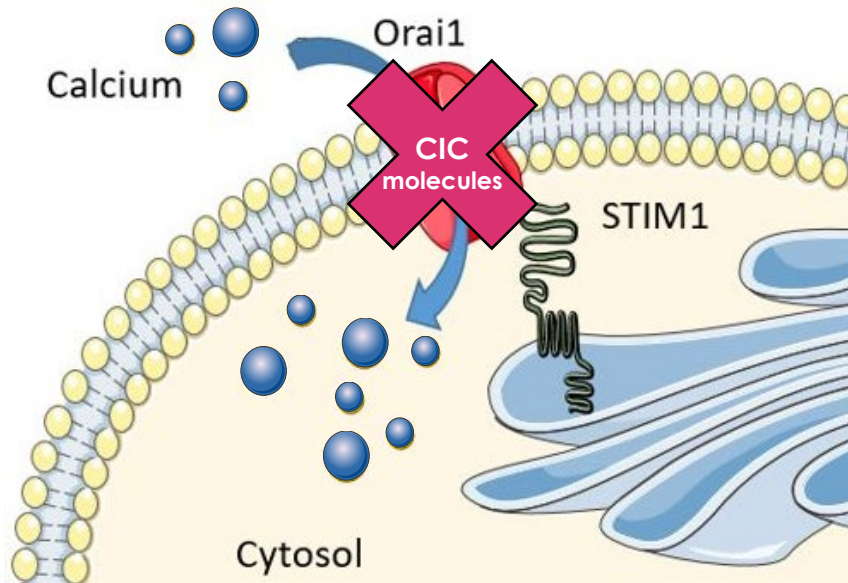


### Novel target in pharmacology

- Few SOCE modulators are in clinical trials
- No SOCE modulator has reached regulatory approval



## Innovative mechanism of action



## 2 novel chemical families of small molecules



IP protected



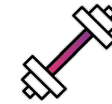
High selectivity



Good safety & PK profile

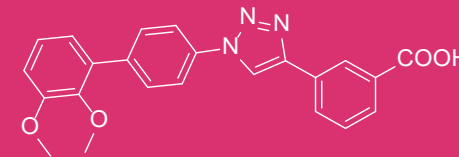


Easy manufacturing



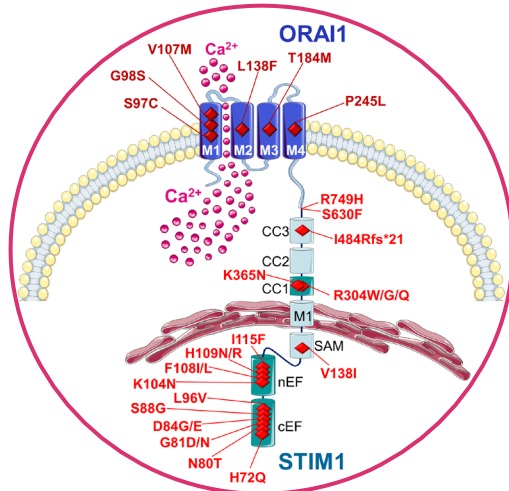
High potency (nM) range

### CIC-39



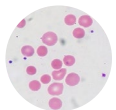
## Tubular aggregate myopathies

Tubular aggregate myopathy, Stormorken syndrome  
York platelet syndrome

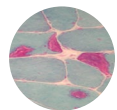


**SOCE over-activation**

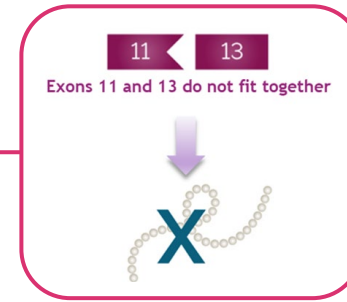
Thrombocytopenia  
Abnormal Bleeding



Muscle stiffness  
Painfull Cramps



## Duchenne muscular dystrophy



**SOCE over-activation**

**Duchenne muscular dystrophy (DMD)**

- Large calf muscles
- Muscle pain and stiffness
- Frequent falls
- Trouble running and jumping
- Learning disabilities
- .....

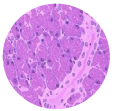
Apoptosis and Necrosis



Muscle damage  
Functional impairment

## Acute pancreatitis

**SOCE over-activation in pancreatic acinar cells (PACs)**

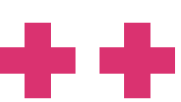


**Intracellular Ca<sup>2+</sup> overload in PACs**

**Uncontrolled release of intracellular digestive proenzymes**

Suden and painfull inflammation of pancreas and peri-pancreatic organs

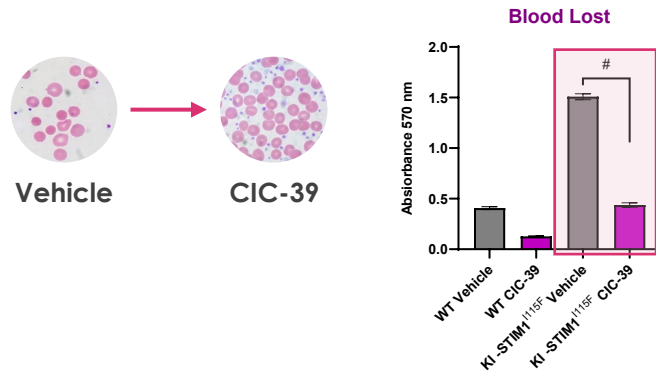




## Tubular aggregate myopathies

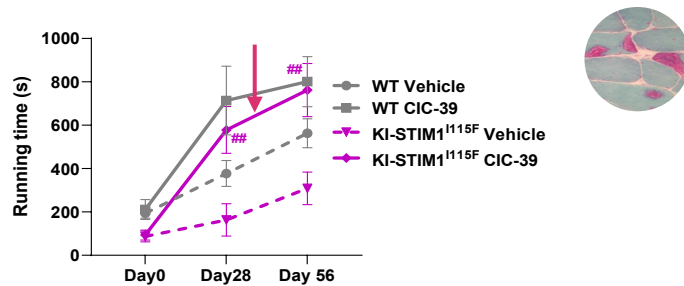
### Reducing blood loss

CIC-39: 60 mg/Kg/daily 15 days



### Contrasting muscle damage

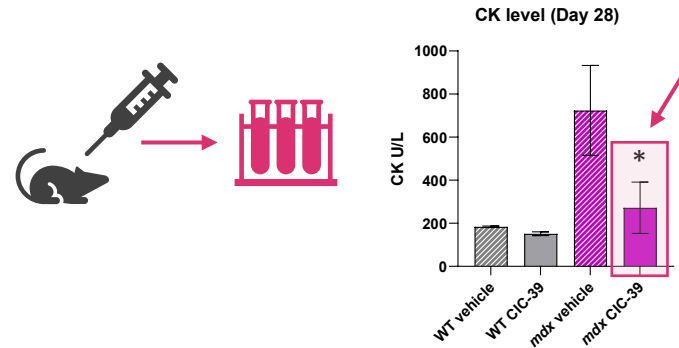
CIC-39: 60 mg/Kg/daily 56 days



## Duchenne muscular dystrophy

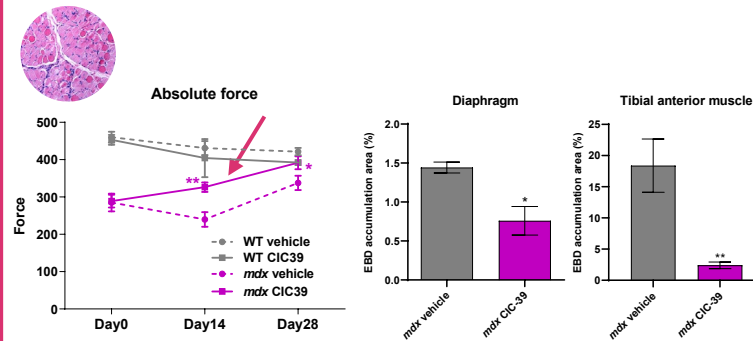
### Reduction of creatine kinase plasma levels

CIC-39: 60 mg/Kg/daily 28 days



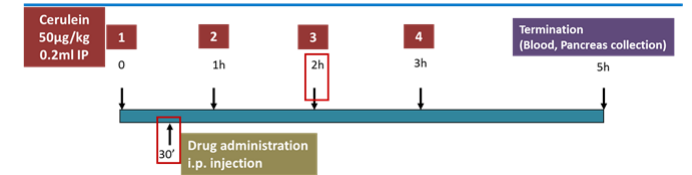
### Contrasting muscle damage & reducing apoptosis

CIC-39: 60 mg/Kg/daily 28 days



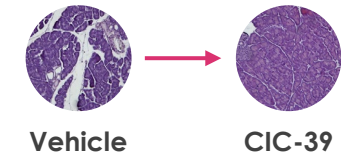
## Acute pancreatitis

### Experimental protocol



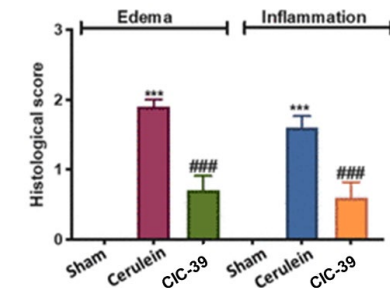
### Restoring pancreatic tissue edema

CIC-39: 10 mg/Kg (x2) IP administration



### Reducing inflammation

CIC-39: 10 mg/Kg (x2) IP administration



Drug	Company	Therapeutic indication	Phase	Status	Reference
CM4620 (Auxora)	CalciMedica	Acute pancreatitis	II	Completed	NCT03709342 NCT03401190
CM4620 (Auxora)	CalciMedica	Acute pancreatitis and systemic inflammatory response syndrome (SIRS)	I II	Recruiting	NCT04195347 NCT04681066 Bruen C., et al. 2021
CM4620 (Auxora)	CalciMedica	Severe COVID-19 Pneumonia	II	Completed	NCT04345614 Miller J., et al. 2020
RP3128	Rizhen Pharmaceuticals	Asthma	II	Terminated (Significant recruitment delay in POC part)	NCT02958982 Barde J., et al. 2021
RP4010	Rizhen Pharmaceuticals	Relapsed or refractory lymphomas	I/IIb	Terminated (Study stopped after reviewing PK and safety results)	NCT03119467
PRCL-02	PRCL Research Inc.	Plaque psoriasis	I/IIa	Completed	NCT03062618 NCT03614078

## CIC-39 vs CM4620



**> Selectivity**  
for SOCE channels



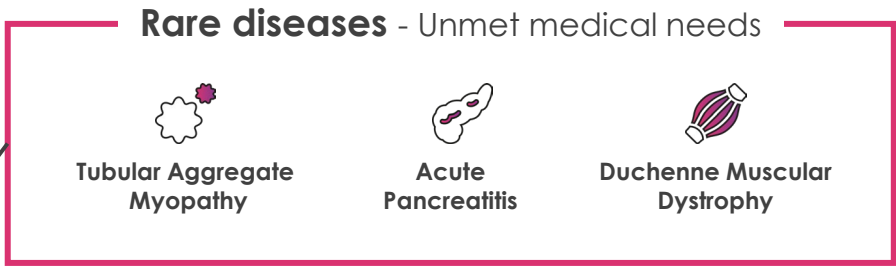
**< Cytotoxicity**  
in acute and chronic conditions



**> Solubility**  
in physiological solution

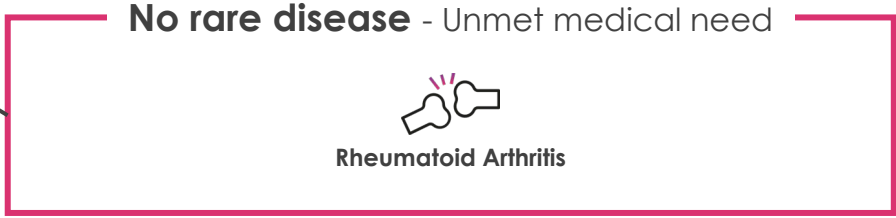


Several SOCE related diseases  
(both rare and no rare diseases)



### Orphan Drugs

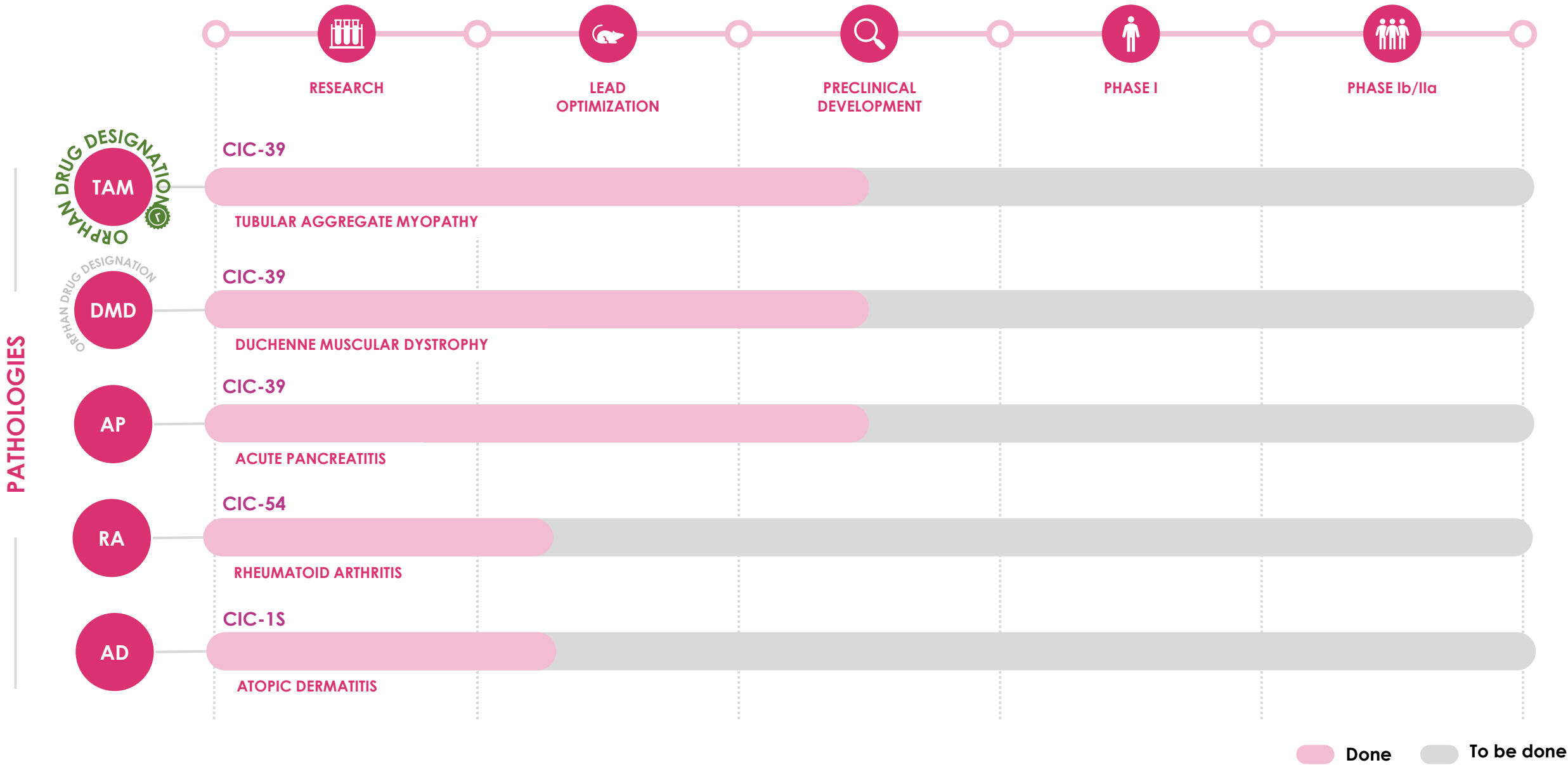
- EMA Advice & Support
- Dedicated Fundings
- 10 Years market exclusivity
- Tax benefits



Further market opportunity

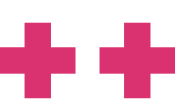
Disease	Incidence	Addressable market	Notes
TAM	1/100,000 (global)	250 M€	Rare genetic disease with childhood onset that affect mainly skeletal muscle and platelets (TAM includes York platelet and Stormorken syndromes).
DMD	1/3,300 (male, global)	365 M€	Rare genetic disease. Lethal and progressive paediatric muscle disorders.
AP	1/2,000 (global)	540 M€	Rare disease characterized by sudden and painful inflammation of pancreas and peri-pancreatic organs.

# R&D pipeline



Done To be done



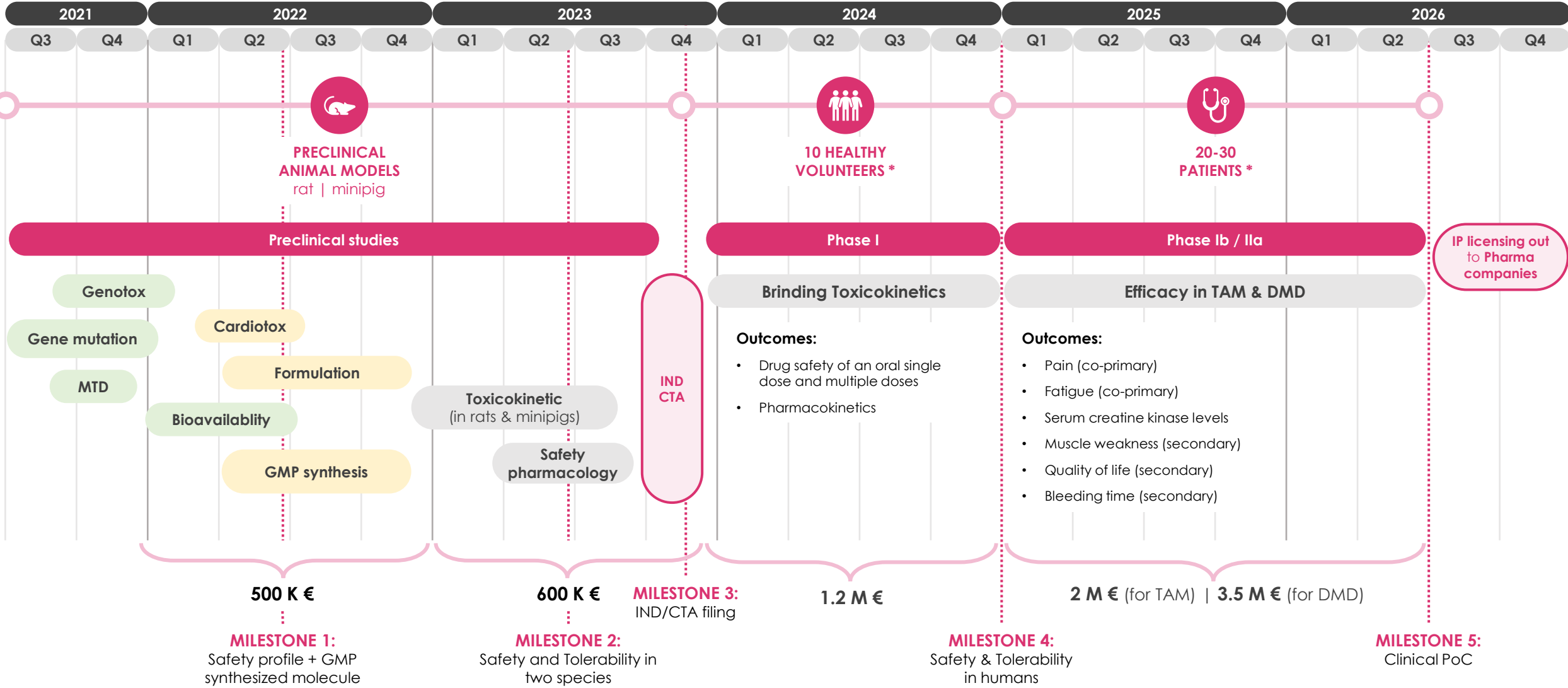


# Development Plan

Done

Ongoing

To be done





**Dr. Beatrice Riva**, PhD  
President & CEO  
Founder



**Dr. Tracey Pirali**, PhD  
CTO,  
Founder



**Dr. Demetra Pelos**  
IP Portfolio Strategy



**Dr. Lucrezia Barone**  
Financial Analyst



**Dr. Simona Somaini**  
Regulatory / QC



**Dr. Marco Gili**  
Legal & General Affairs

## Scientific Collaborators

**Prof. Armando Genazzani**, MD, PhD  
Pharmacologist



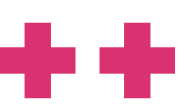
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Clinical expert in myopathies



SAPIENZA  
UNIVERSITÀ DI ROMA

**Prof. Nicoletta Filigheddu**, PhD  
Clinical expert in dystrophies





## Research Institutions & Business Partners





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