

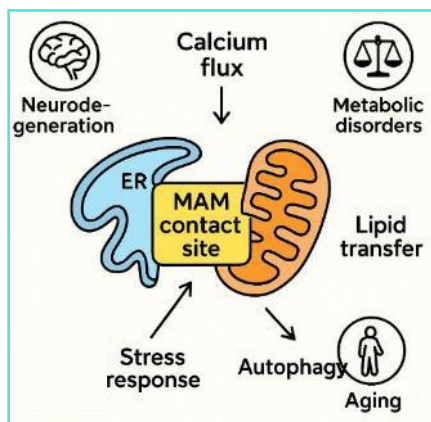


Sitera
Pharmaceuticals

Driving Innovation, Delivering Hope.

SITERA Biotech Executive Summary

Targeting the **Mitochondria-Associated Membranes (MAM)** : a key hub in cell metabolism



MAM **Dysfunction** in
Neurodegenerative diseases

**Elevated ROS
production**

Mitophagy

MAM **Targeting** :
Targeted therapies
Mitochondrial health
Neuroplasticity

SITERA operates a **unique, cutting-edge** technological platform in **neurosciences**, designed to :

Generate potential *first or best-in-class* candidates

Address MAM dysfunctions and restore cellular impairments

Provide therapeutic solutions for **neurodegenerative diseases**

1



Focus on rare and less rare neurodegenerative diseases : Wolfram syndrome, Charcot-Marie Tooth 2A, ALS but also Alzheimer's and Parkinson's disease. **Total market size** : 65G\$ by 2030

2



Strong and large IP portfolio encompassing 2 patents (2021 on the target, 2025 - Composition of matter), a pipeline of +300 New Chemical Entities distributed in 3 chemical series

3



PoC with Wolfram syndrome and rapid extension to other diseases
This strategy is supported by common target&MOA and conclusive *in vivo* Proof-Of-Concept on preclinical animal models

4



Orphan Drug/Fast Track Designation

Our drug candidate SIT3060 addresses an unmet medical need as there is no treatment available to treat Wolfram Syndrome

5



Financials: Looking for 15 M€ to complete regulatory preclinical up to clinical Proof-Of-Concept for SIT3060, our drug candidate in Wolfram syndrome

The Huge Medical Need for Wolfram Syndrome

The Wolfram syndrome is a well-characterized ultra-rare disease with no treatment available

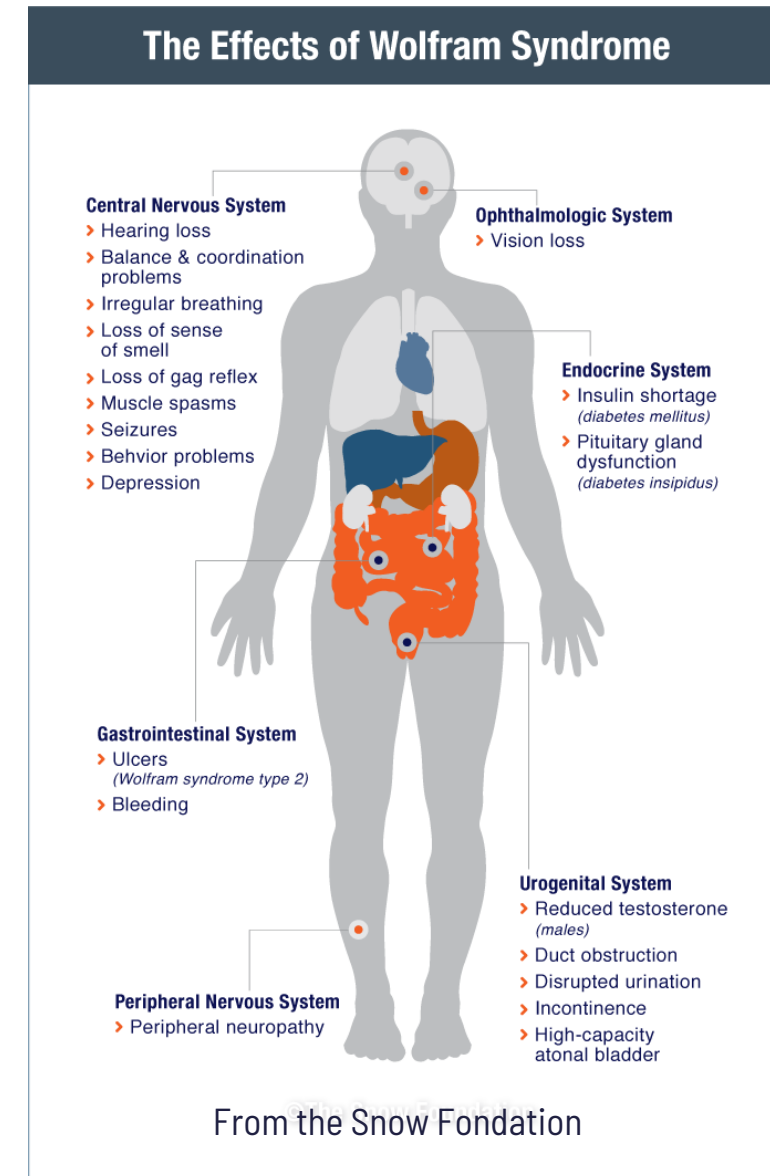
Monogenic **rare disease** WFS1 gene mutation coding for **wolframin**

Characterized by juvenile type1/insipidus **diabetes**, an **optical atrophy** and a **hearing loss** (DIDMOAD)

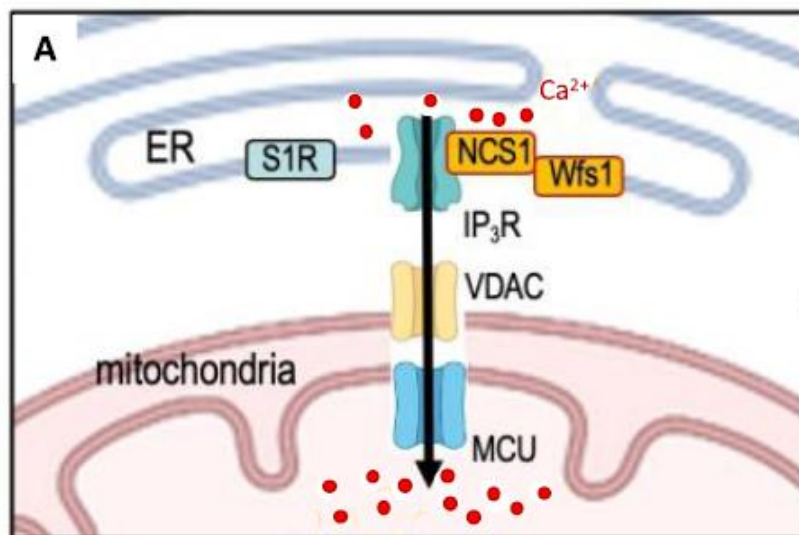
1 child over **55 000** to **770 000** affected worldwide

The **disease** progresses to significant **neurodegeneration** and patients **die** around the **age of 35**

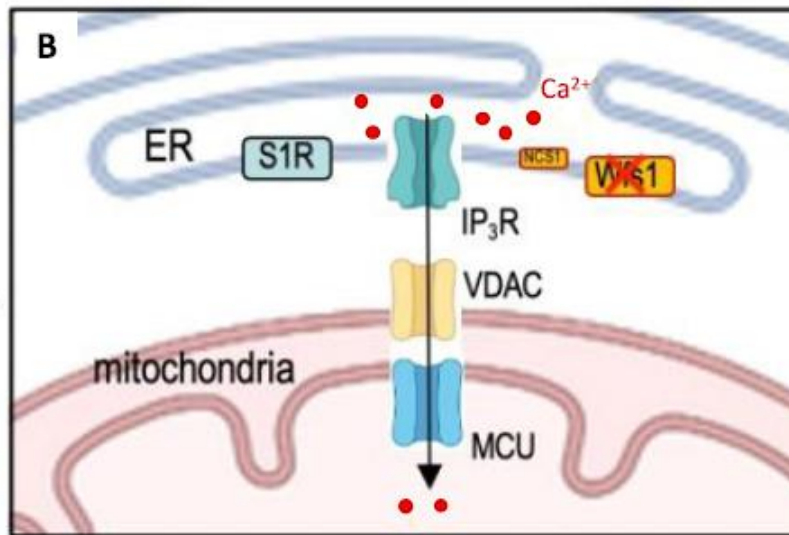
Patients are at a therapeutic impasse due to the lack of effective treatments



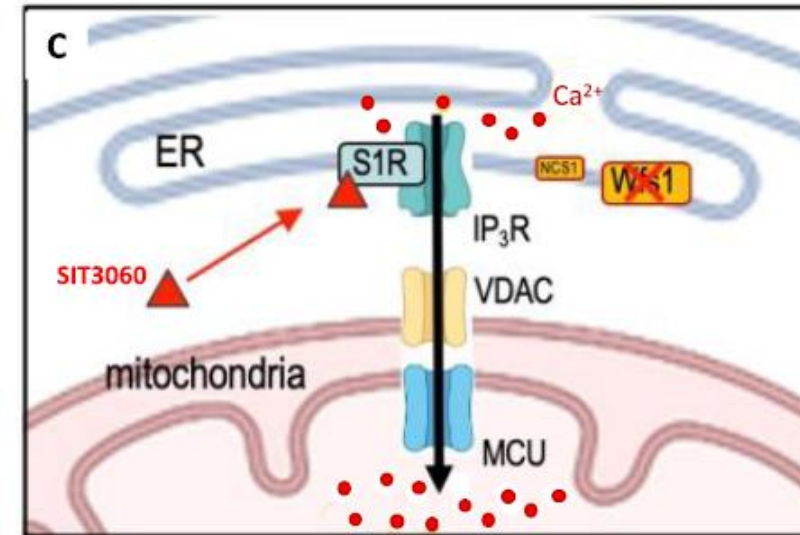
Wolfram syndrome is an altered ER-mitochondria communication that can be corrected by a S1R agonist



Physiological condition



Patient with Wolfram syndrome



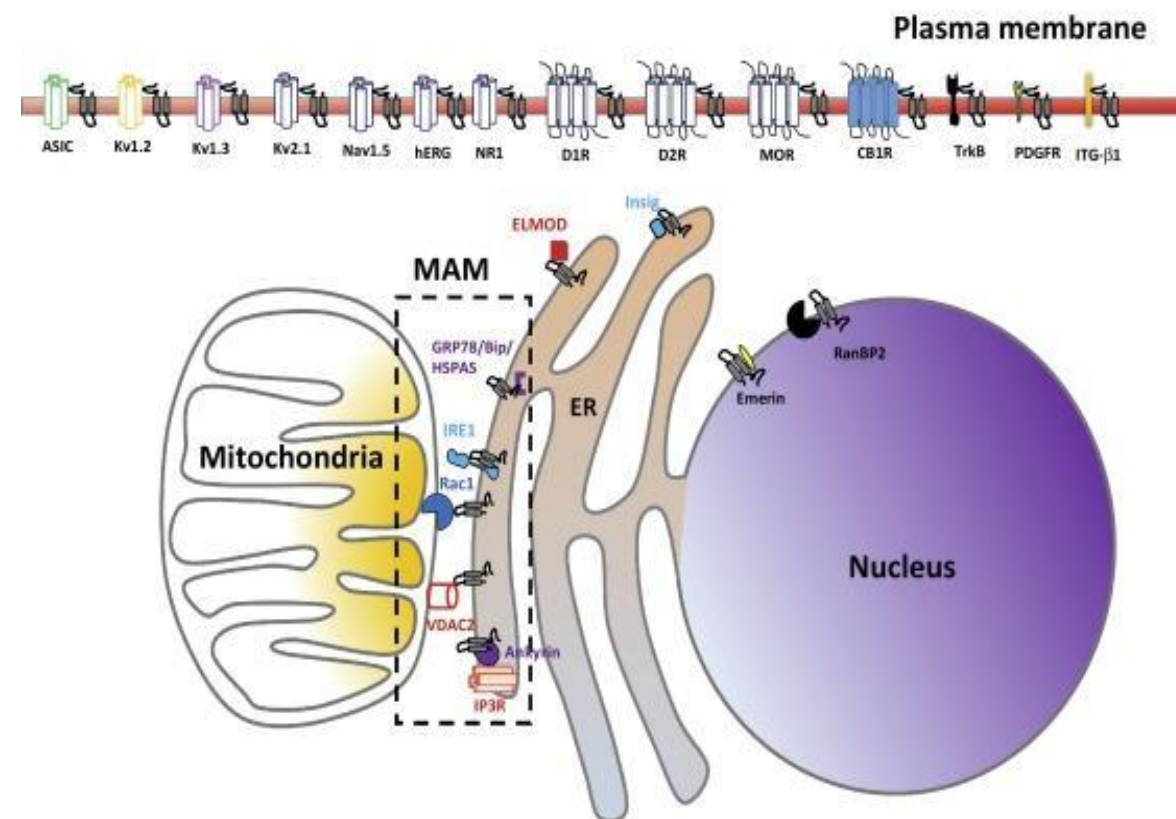
Patient with Wolfram syndrome

▲ Treated with a sigma-1 receptor agonist

IP3 receptor stabilization
ER/mitochondria restored communication
Increased calcium transfer

The sigma-1 receptor is a key therapeutic target acting as a neuroprotective protein chaperone

- Highly conserved transmembrane **chaperone protein**, operated by ligands
- **Mostly found in Mitochondria Associated Membranes (MAMs)**, but also on endoplasmic reticulum, nuclear and plasma membranes
- Regulates **calcium homeostasis** between endoplasmic reticulum and mitochondria
- **Reduces oxidative stress** and support mitochondria function
- Interacts with ion channels and signaling proteins, promoting **neuronal survival** and reducing excitotoxicity
- Support lipid and protein trafficking at MAMs



Su et al, TIPS **2016**

The sigma-1 receptor is a clinically validated target in several neurodegenerative diseases

Disease	Prevalence worldwide	Molecule Preclinical/ clinical	Stage	References
Alzheimer	58 M (2019) 139 M (by 2050)	PRE-084 Donepezil ANAVEX3-71 (AF710B) Pridopidine (ACR16) Edonerpic maleate (T-817MA) Blarcamesine (ANAVEX2-73)	Discovery Marketed Preclinical Preclinical Phase II Approval	Marrazzo et al, NeurReport 2005 Meunier et al, BJP 2006 Fisher et al, Neurodegen Dis 2016 Estévez-Silva et al, Neurother 2022 Fukushima et al, BBRC 2011 Villard et al., JOP 2011
Parkinson	8.5 M (2019) 25 M (by 2050)	PRE-084 Pridopidine (ACR16) Blarcamesine (ANAVEX2-73) Afobazole dextromethorphan	Discovery Phase III Phase III Discovery Discovery	Francardo et al, Brain 2014 Johnston et al., Mov Disord 2019 Voronin et al., Sci Rep 2019 Kadnikov et al, IJMS 2020 Liu et al, EJP 2019
Huntington	400-800 K <i>estimated</i>	PRE-084 Pridopidine (ACR16) 3-PPP	Discovery Phase III Discovery	Hyrskyluoto et al, CDD 2013 Ryskamp et al, Neurobiol Dis 2017 Bol'shakova et al, CTBM 2017
ALS	222 K (2015) 376 K (by 2040)	PRE-084 Cutamesine (SA4503) Pridopidine (ACR16)	Discovery Discovery Phase II	Mancuso et al, Neurother 2012 Ono et al, NSL 2014 Estevez-Silva et al, EJN 2022

SITERA timeline and major achievements

DISCOVERY STAGE 2002-2020	MATURATION STAGE 2020-2024	START-UP 2024-2026	PRECLINICAL STAGE 2026-2028
Fundamental research (target, pathologies) 2002 – Target identification 2011 – Sigma-1 agonists neuroprotective effect 2015 – Sigma-1 agonists mitoprotective effect 2015 – Wolfram syndrome program initiation  3 M€	Fundamental research (mechanism) Publication in Sci. Trans. Med. 1st patent (target) Medicinal chemistry program Generation of a pipeline of NCEs Hit-to-lead and lead ID (SIT3060)  1.4 M€	SITERA incorporation Structuration of the therapeutic platform 2nd patent (comp. of matter SIT3060) Completion of SIT3060 preclinical data package  685 K€	CMC program (GMP batches) GLP toxicological studies Safety pharmacology CTA submission Design of SITERA clinical trial in Wolfram syndrome 3rd patent (new chemical series)  Fundraising ongoing

Total funding to date : approx. 5 M€

Funding from academic partners : 4.4 M€

Non-dilutive funding : 685 K€

**SITERA was recently funded by
European Rare Disease Research
Alliance (ERDERA, 500 K€)**

ERDERA
European Rare Diseases
Research Alliance

A complementary Team and key Experts

Staff Members



Henri PIRAS
CEO - *Co-founder*
Ph.D in MedChem
>10 y experience
in **Drug Dev**



Christine PLACET
CFO - *Co-founder*
Extensive experience in
neurosciences biotechs



Benjamin DELPRAT
CSO - *Co-founder*
Research Director INSERM
Expert in the biology of
neurodegenerative diseases



Tangui MAURICE
CTO - *Co-founder*
Research Director CNRS
Expert in the **therapeutic target**



Johann MEUNIER
Senior Project Manager

Scientific co-founders



David VIRIEUX
Research Director CNRS
Co-founder
Expert in Medchem (target related)



Tahar AYAD
Research Associate CNRS
Co-founder
Medicinal and organic chemist



Jean-Luc PIRAT
Research Director CNRS
Co-founder
Expert in Medchem (target related)

Experts



Didier CUSSAC
Drug Dev. Expert



David BANCROFT
IP counsel
dab / IAS

Funding Partners



SITERA is supported by a network of patient associations and clinicians to design its clinical trial on Wolfram syndrome

 **French Association**
for Wolfram Syndrome



 **Eye Hope Foundation**
for Wolfram Syndrome



 **Snow Foundation (US)**
for Wolfram Syndrome



 **Tiger Foundation (US)**
for Wolfram Syndrome

Be a *Tiger*
Foundation



 **Hôpital européen**
Georges-Pompidou
AP-HP

Christophe ORSSAUD
Head of the reference center on WS



UNIVERSITY OF
BIRMINGHAM

Timothy BARRETT - Top 1 KOL WS
Director, Center of Rare Diseases

CHU

MONTPELLIER
CENTRE
HOSPITALIER
UNIVERSITAIRE

Agathe ROUBERTIE
Head of the reference center on WS



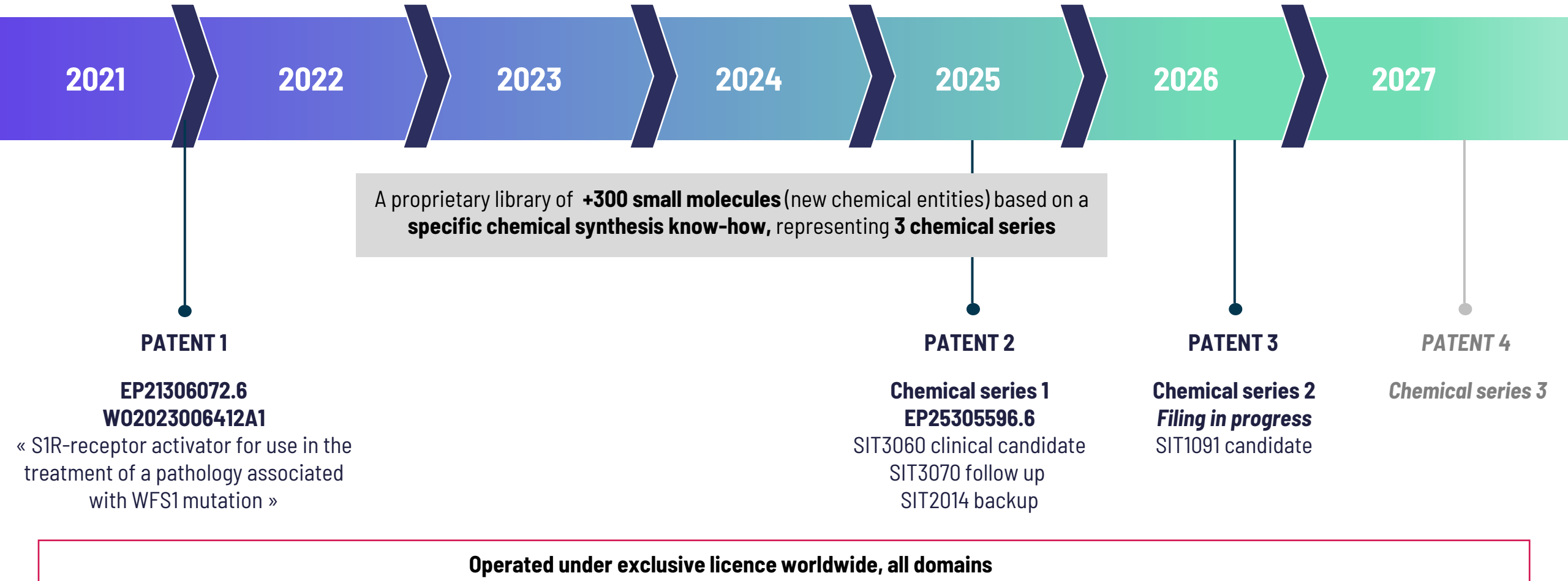
Gema ESTEBAN BUENO
Clinical Expert on WS



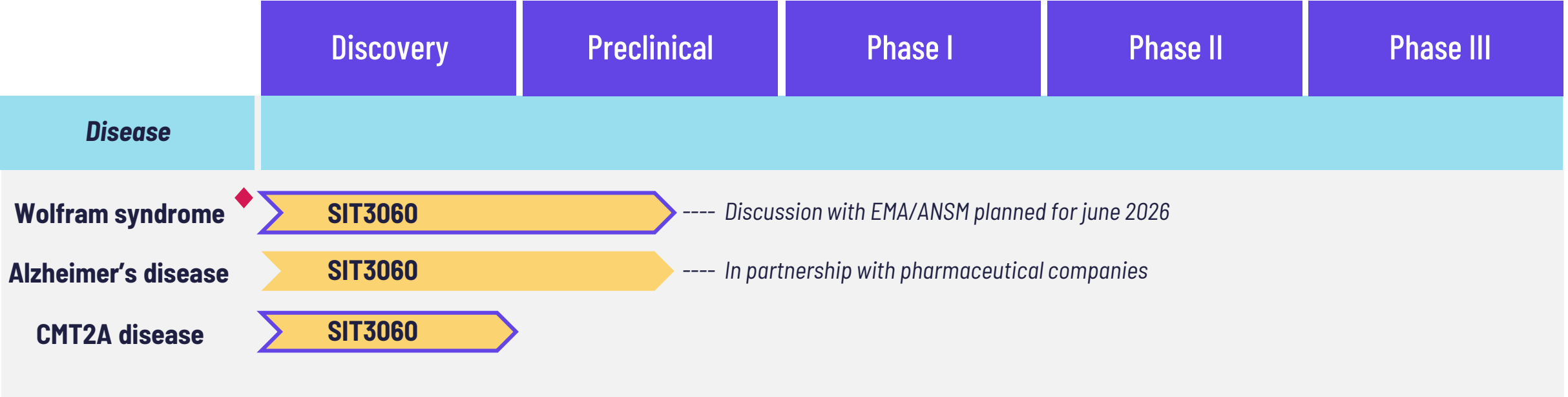
MEDICAL
UNIVERSITY
OF LODZ

WOJCIECH Mlynarski
Clinical Expert on WS

SITERA Industrial Property Assets



SITERA is expanding its pipeline for neurodegenerative diseases



 Rare disease

◆ Orphan Drug Designation application

SIT3060 : Efficacy Proof-Of-Concept validated in preclinical Wolfram syndrome models

In vitro

Cellular model :

- SIT3060 protects Wfs1^{KD70} MIN6 bêta-pancreatic cells from glucose-induced toxicity and increases insulin secretion
- SIT3060 protects against glucose-induced oxidative stress in Wfs1^{KD70} MIN6 bêta-pancreatic cells

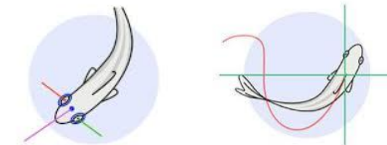
Wolfram Patient's fibroblasts :

- SIT3060 corrects the altered oxygen consumption rate until levels equivalent to healthy subjects
- SIT3060 corrects the altered mitochondrial calcium uptake until levels equivalent to healthy subjects

In vivo

Wfs1^{abKO} zebrafish model :

- SIT3060 completely reverses the hyperlocomotor VMR response in Wfs1^{abKO} zebrafish larvae



Wfs1^{E884K} mice model :

- SIT3060 attenuates the altered motor coordination in Wfs1^{E884K} mice
- SIT3060 attenuates the dysregulated glycemic response in male Wfs1^{E884K} mice



Rotarod experiment



SIT3060 : A safe and derisked clinical candidate

Our preclinical data package

- ✓ **Pharmacology – on/off target** Binding mode, affinity and potential off-targets well characterized, showing an excellent selectivity for S1R receptor
- ✓ **ADME *in vitro/in vivo*** Physico-chemical properties, stability&metabolic profile, PK parameters, oral bioavailability
- ✓ **Safety** No toxicity and adverse effect observed in the studies below:



SafetyScreen 87
Panel CEREP



Cytotoxicity
(hepatic primary
cell lines)



Cardiotoxicity
(isolated perfused
heart)



Zebrafish larvae
toxicity



Non-GLP tox
7 days on mice



Histopathological
study

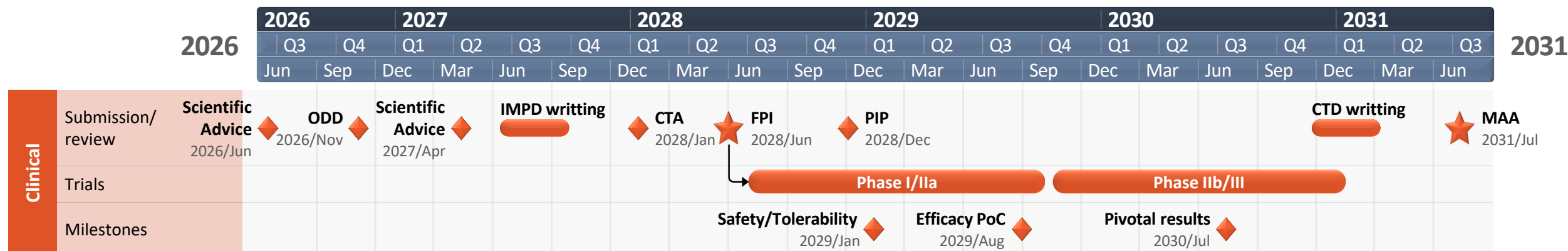


Genotoxicity
(AMES package)

The next steps

- Ensure the pharmaceutical developability (**CMC**) of the clinical candidate
- Provide **GMP batches of drug candidate** to conduct regulatory **preclinical** and **clinical studies**
- **Complete** and **file CTA**

Our clinical roadmap for SIT3060 in Wolfram syndrome



Rare disease with no approved treatment > ODD

Fast Track and Priority review

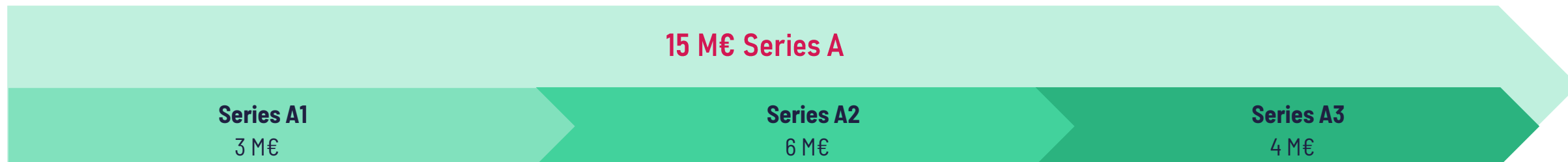
**Conditional approval (Europe)
Compassional use (France)**

- EMA/ANSM **Scientific Advice planned for June 2026** to get a general approval on the design of our preclinical and clinical studies
- **Orphan Drug Designation** during preclinical development
- Interaction with PDCO and **PIP submission** to integrate juvenile cohort (6-12 yo patient) in PhIIb/III
- Support **conditional approval** with surrogate endpoint and early clinical data

SITERA favourably positioned in the competitive landscape of Wolfram Syndrome treatment

Company/ Sponsor	Product	Development stage	Mechanism Of Action	Our analysis
Fumihiko URANO	Dantrolene <i>repurposing</i>	Phase II	Ryanodine receptor	No <i>in vivo</i> preclinical data Negative results from PhII trial
Christophe ORSSAUD	Valproate <i>repurposing</i>	Phase II AUDIOWOLF trial	P21 CIP1	No <i>in vivo</i> preclinical data Expected results publication in 2027
Tim BARRETT	Valproate <i>repurposing</i>	Phase II TREATWOLF trial	P21 CIP1	No <i>in vivo</i> preclinical data Negative results from PhII trial
 AMYLYX®	AMX0035 <i>Relyvrio</i>	Phase II HELIOS trial	ER stress Apoptosis	Glycemia/insuline toxicity as sole readout
 prilenia	Pridopidine	Preclinical	Sigma-1 R agonist	Pridopidine shows no effect on our wfs ^{1KO} zebrafish preclinical model
 Sitera Pharmaceuticals	SIT3060	Preclinical	Sigma-1 R agonist	SIT3060 efficacy validated in Wolfram syndrome murine preclinical models and patient-derived fibroblasts

Fundraising structuration – Scenario 2



Allocation

- CMC initiation (first GMP-like batch)
- Non-regulatory preclinical studies (late DMPK, DRF)
- Scientific Advice meeting with EMA/ANSM

Key achievements

- Industrial synthetic process for SIT3060
- Dose Range Finding in relevant animal species
- Feasibility assesment&validation of clinical plan
- ODD for SIT3060

Allocation

- Preparation of GMP batches
- Regulatory preclinical studies (general toxicity, toxicokinetics...)
- Safety pharmacology
- CTA filing

Key achievements

- CTA
- First-In-Human for SIT3060

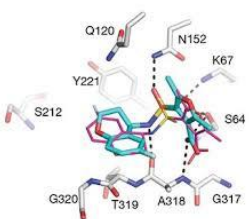
Allocation

- Clinical trial phase I
- Clinical trial phase II

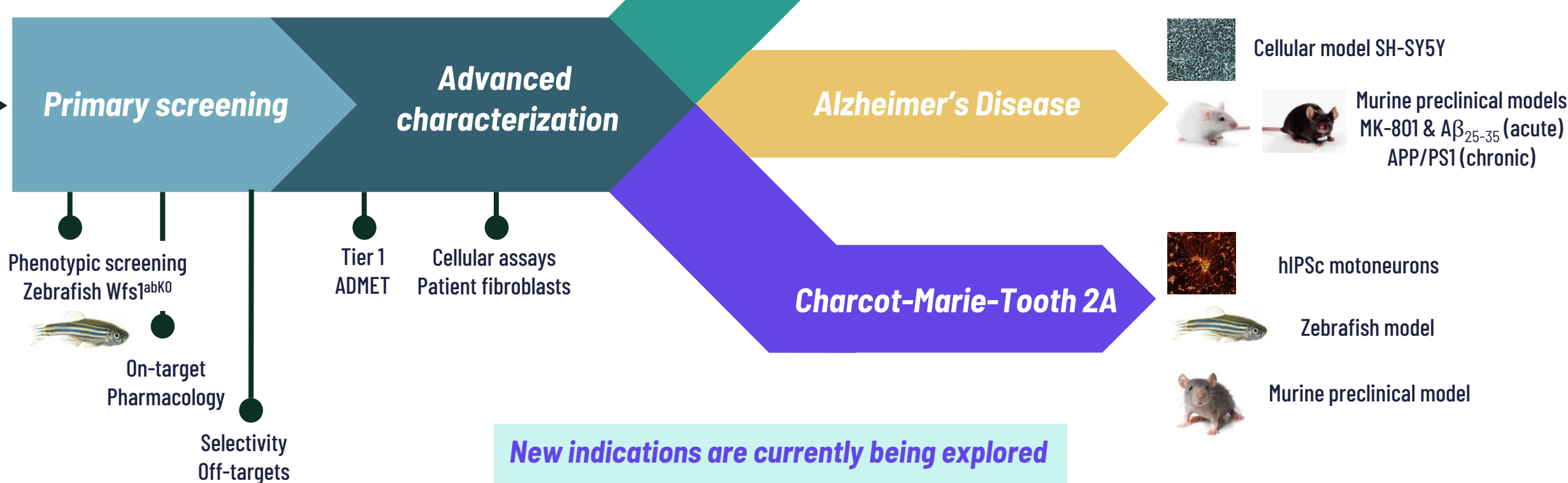
Key achievements

- First-In-Human for SIT3060
- Safety&Tolerability assessment
- Pediatric Investigation Plan
- Clinical efficacy Proof-Of-Concept in Wolfram syndrome

Our technological platform relies on a combination of *in vitro/in vivo* internalized preclinical models and pharmacological characterization



Proprietary NCEs



SIT3060 : Efficacy Proof-Of-Concept validated in preclinical Alzheimer's disease models

In vitro

Cellular model :

- SIT3060 protects SH-SY5Y cell lines against $A\beta_{25-35}$ -induced cytotoxicity
- SIT3060 protects CHO cell lines against $A\beta_{25-35}$ -induced cytotoxicity

In vivo

Dizocilpine-induced learning impairment mice model

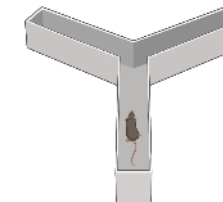
- SIT3060 fully prevents dizocilpine-induced spatial working memory deficit in mice tested in the Y-maze spontaneous alternation and passive avoidance tests

$A\beta_{25-35}$ -induced learning impairment mice model (acute)

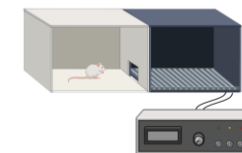
- SIT3060 fully prevents $A\beta_{25-35}$ -induced spatial working memory deficit in mice tested in the Y-maze spontaneous alternation and passive avoidance tests
- SIT3060 fully prevents long term $A\beta_{25-35}$ -induced spatial working memory deficit in mice and acts as disease modifier

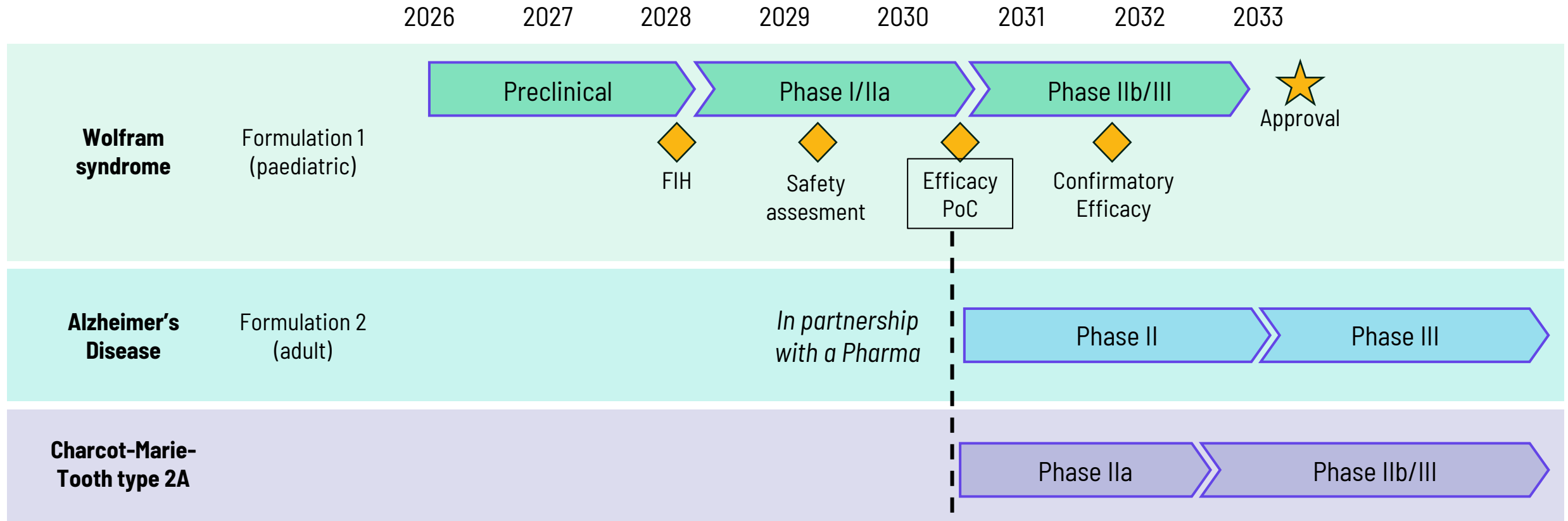
APP/PS1 transgenic mice model (chronic) - ongoing

Spontaneous alternation



Passive avoidance





Potential exit strategies for investors

- Industrial partnership with a view to a potential acquisition of the platform
- Industrial partnership and IPO –risk mitigation and value creation

Examples

SANOFI <> Vigil Neurosciences	470 M\$ upfront
Jonhson&Johnson <> Intra-cellular Therapies	14.6 Mds\$
Biocodex <> THX Pharma	173 M€

Why invest in SITERA now ?

- SIT3060 with demonstrated efficacy and safety **is entering in regulatory preclinical phase**
- SIT3060 addresses an **unmet medical need** as there is **no treatment available** for Wolfram Syndrome
- Our partnership with patient associations and clinicians **accelerates** SIT3060 **entry into clinical phases by 2028**
- Opportunity **to extend SIT3060 application** in larger neurodegenerative diseases (supported by strong scientific validation and robust preclinical data)
- **High potential** for our technological platform to deliver **validated clinical candidates** in multiple neurodegenerative diseases (based on common target and MoA)

We are seeking to raise 15 M€ to complete IND/CTA-enabling studies and regulatory preclinical up to clinical Proof-Of-Concept for SIT3060 in Wolfram syndrome



Sitera

Pharmaceuticals

Contact us !

Henri PIRAS - CEO

henri.piras@siterapharma.com



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