28 de noviembre de 2023

ONR-001, first-in-class oral treatment to overcome cancer persistence

Esther Riambau

Content

ONIRIA® THERAPEUTICS

Modulating cell dormancy to overcome cancer persistence

VHIO Vall d'Hebron Institute of Oncology

Universitat de Barcelona Spin-off

ICREA

Mind the Gap | Fundación Botín

Sabadell BStartup

CORE FOUNDERS TEAM

A solid team combining expertise in drug discovery, oncology and business management

Esther Riambau, MBA
Chief Executive Officer & Board Member

- >19 years in **Technology Transfer**
- Co-founder & Board Member at Gate2Brain Spin-off company
- Member of the Steering Committee of i4Kids (Pediatric's Hospital Accelerator)

Héctor G. Palmer, PhD
Chief Scientific Officer & President of the Board

- Head of the Stem Cells and Cancer Group at VHIO
- 25 years in cancer biology research & **Drug Resistance**
- >15 years developing drugs with pharmaceutical industry
- Generation of patient-derived cancer models

Isabel Puig, PhD
Head of Drug Target Discovery & Validation

- >20 years studying mechanisms of tumorigenesis
- **TET2 specialist**

Josep Tabernero, MD, PhD
Chief Medical Advisor

- VHIO & Caixa Research Institute Director
- Head of **Medical Oncology** Department at Vall d´Hebrón Hospital
- Former ESMO president
- World reference in clinical development of new drugs in oncology

Xavier Barril, PhD
Computational Chemistry & Drug Discovery

- ICREA Research Professor at University of Barcelona
- Head of **Computational Biology** and Drug Design Group
- Vernalis R&D
- Serial Entrepreneur: Minoryx Therapeutics & Gain Therapeutics

Carles Galdeano, PhD
Targeted Protein Degradation & Drug Discovery

- Head of **Protein Degradation** (PROTAC) Lab at University of Barcelona
- Expert in Medical Chemistry

TEAM EXPANSION & CONSOLIDATION

BUSINESS MANAGEMENT

Jordi Petit, MBA
Chief Financial Officer

- >20 years of experience as an entrepreneur, CEO, CFO and investor
- Currently Senior Manager at Deloitte

Marc Ramis, MBA
Business Strategy Advisor

- Co-founder and Partner at Chasing Science and Manor House
- Serial entrepreneur & Board Member or Strategic Advisor several companies
- Venture Partner at Ship2B Ventures and Korion Life Sciences
- Currently he is growing a new Venture to Impact Children's Health

Natalia Ricco, PhD
Innovation Manager

- >10 years of experience managing competitive funds
- PhD and Postdoc in oncology

SCIENTIFIC RESEARCH

Elsa Martínez, PhD
Senior Chemistry Scientist

Tuo Chen
Chemistry Technician

David Aguilar, PhD
Cancer Biology Scientist

Iris Marcote
Cancer Biology Tech

Laia Cabellos
Laboratory Manager

Clara Diaz
Cancer Biology Tech

ADVISORY BOARD

Xavier Luria, PhD
Regulatory Affairs

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DMPK

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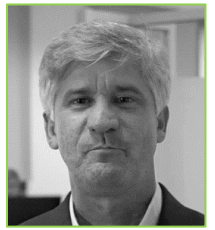
Pharmacology

Julio Castro, PhD
Medicinal Chemistry



Francesc Bosch, MD, PhD
Hematooncology

Diego Muñoz-Torrero, PhD
Medicinal Chemistry

ONIRIA® THERAPEUTICS

THE PROBLEM

The Awakening of Dormant Tumor Cells

Current therapeutic drugs have significantly benefited cancer patients. Unfortunately, most of those who become **RESISTANT to TREATMENTS**, relapse, metastasize and die. Drug-tolerant and **DORMANT TUMOR CELLS** are responsible for **CANCER PERSISTENCE.**

90%

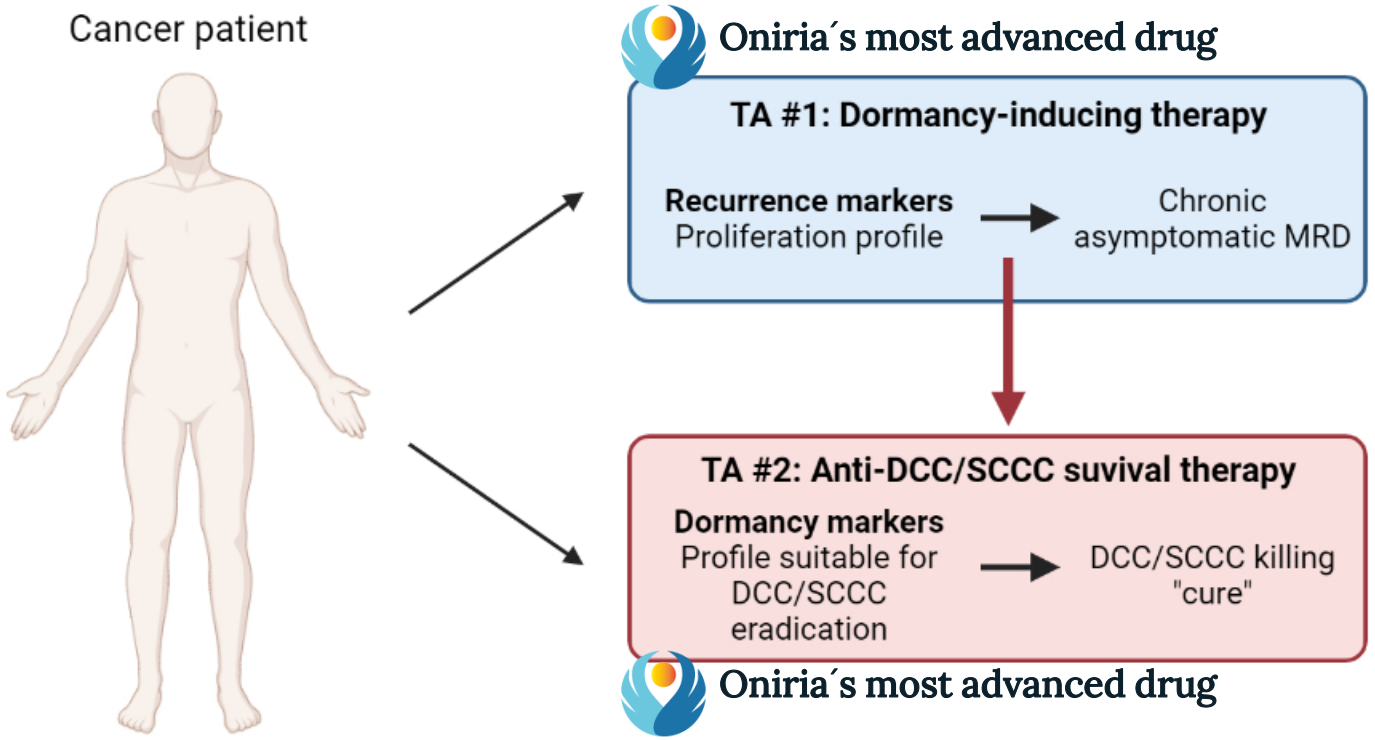
of patients die of CANCER RECURRENCE

10%

of patients die of PRIMARY CANCER

THE STRATEGY

Modulating cell dormancy to overcome cancer persistence



Adapted from Nowacek A and Rigby AC, *Nature Sponsored Feature*, 2019

ONIRIA THERAPEUTICS

OUR MOST ADVANCED DRUG

First-in-class Small Drug TET2 Activator

ONR-001 is a first-in-class small molecule that **allosterically activates TET2**, a master epigenetic enzyme, causing tumor cells to **enter a dormant state and die**.

This unique method can be successfully used at **all stages of the disease**, from naïve primary tumors to recurrent resistant metastatic cancer – thus "making a world of difference".

Oral Efficacy

Small molecule (MW400, LOGP 3,5)
Good potency (sub-µM)
Efficacy in animal models of cancer

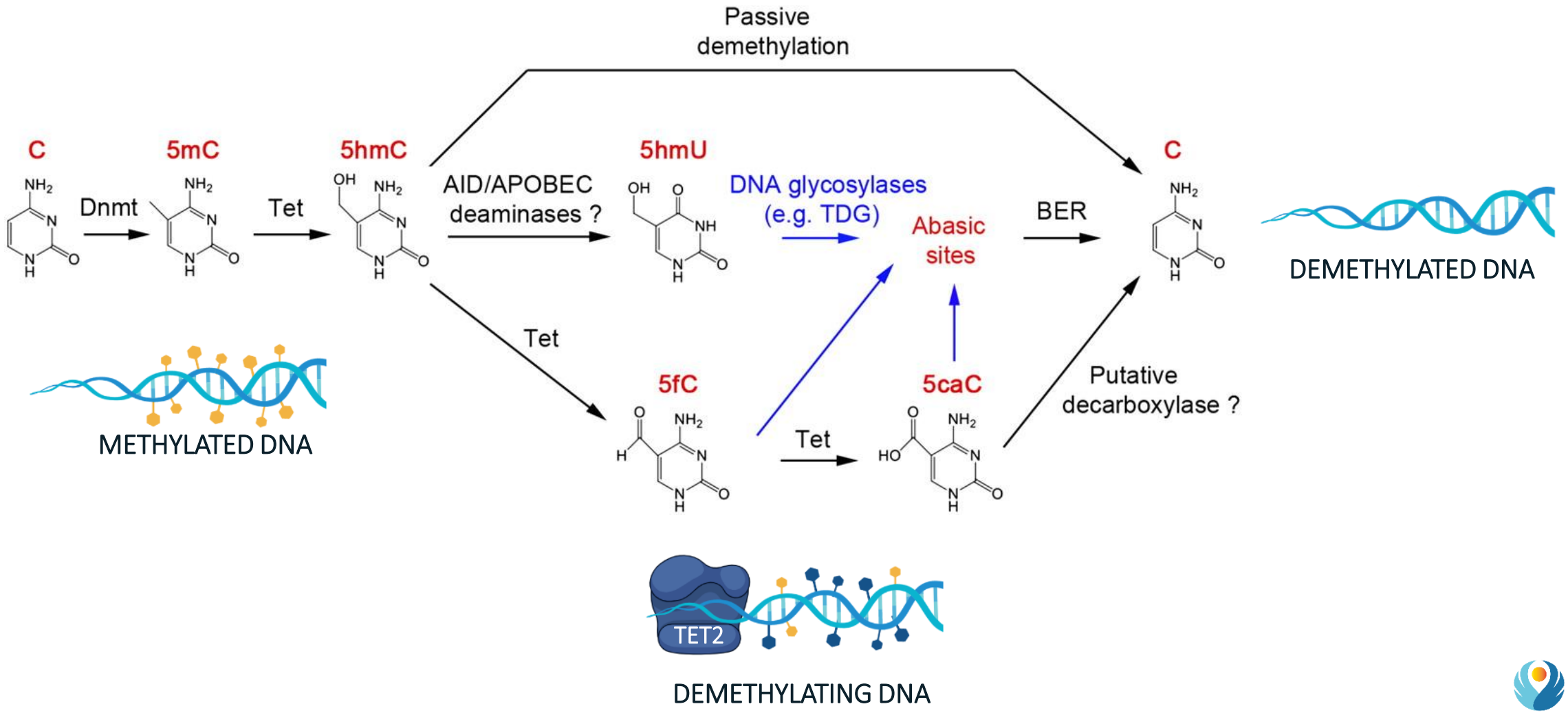
Reaches the target

Crosses the cell and nuclear membranes
Activates TET2 in vivo and in the tumor tissue

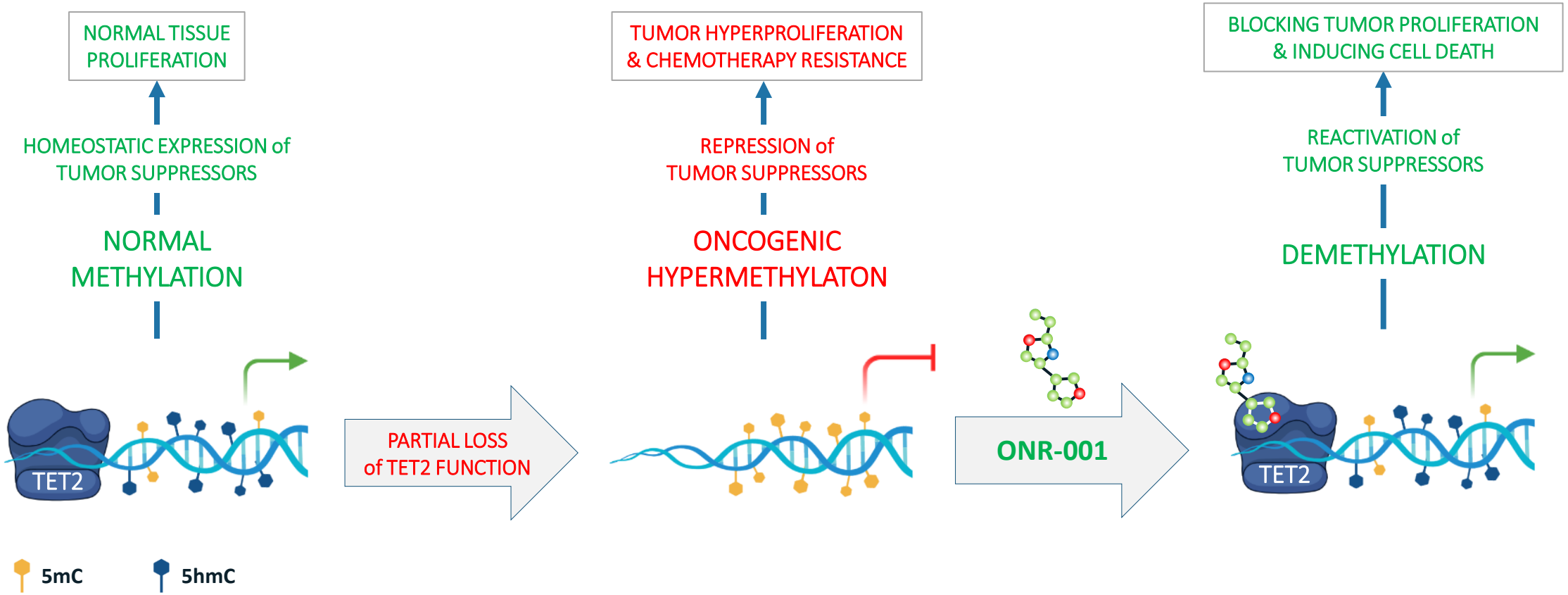
Safe

Target Selectivity
High Acute & Chronic Tolerability in rodents
Clear PK/PD relationship

TET dioxygenases demethylate DNA for gene expression activation



ONR-001 is a first-in-class small molecule activator of TET2

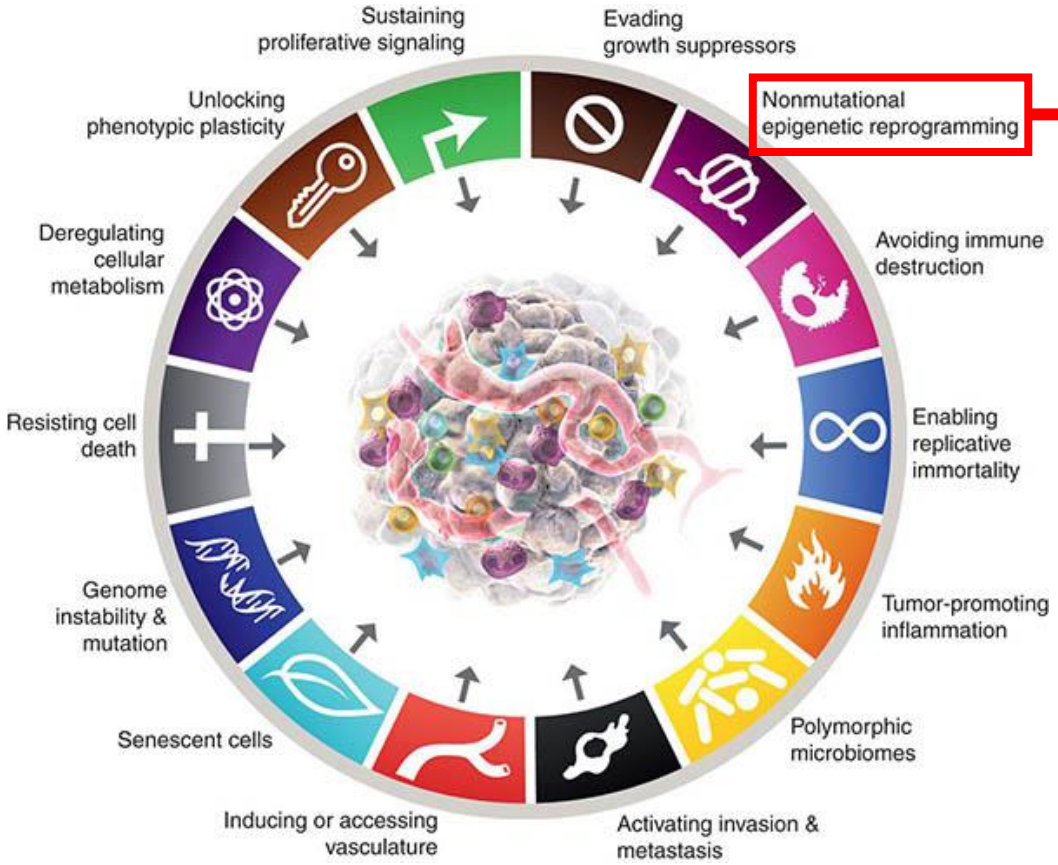


ONR-001 is a specific demethylating agent

TET2 MECHANISM of ACTION

Epigenetic DNA hypermethylation is an essential hallmark of cancer

CANCER HALLMARKS



ONCOGENIC HYPERMETHYLATON

e.g. Tumor suppressor genes

Many tumors affected by hypermethylation:

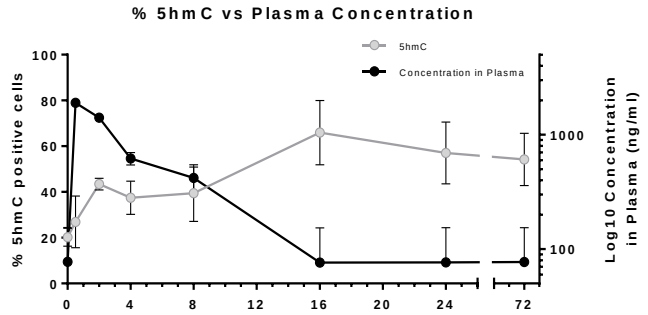
- **HEMATOLOGIC** cancer,
- **COLORECTAL** cancer,
- **MELANOMA**,
- **PROSTATE** cancer,
- **GASTRIC** cancer,
- **GLIOBLASTOMA,** etc.

ONIRIA THERAPEUTICS

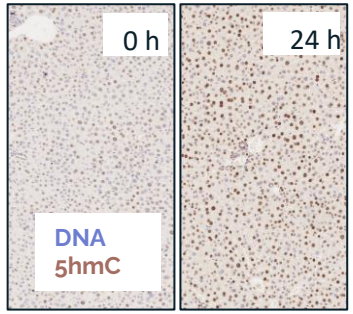
ORAL ABSORTION, LOW TOXICITY & DIFFERENTIAL FEATURES FACING THE MARKET

ONR-001 is a safe molecule with optimal properties for oral administration

A



B



A & B. ONR-001 has an ideal oral PK profile (in-vivo)

SINGLE DOSE /ACUTE TOXICITY of ONR-001 in MICE - EXPERIMENT DESIGN

11 SWISS mice were used in this study, being divided in 2 groups: Vehicle (n=5) and Test Item (n=6). Mice received 1 single oral dose of **250 mg/Kg** of Test Item.

CONCLUSIONS

1. A single oral administration of Test Item at 250 mg/kg only caused mild symptomatology which was reversed before the end of the study (14 days after administration).
2. The absence of relevant injuries in the clinical pathology or histopathology allows us to conclude that the experimental procedure has not caused evident signs of acute toxicity or is pathologically significant.
3. Change of urine colour was observed in both experimental groups, being this effect probably caused by the vehicle.

SUBCHRONIC TOXICITY OF ONR-001 in MICE - EXPERIMENT DESIGN

40 SWISS mice were used in the Main study, being divided in two experimental groups: Vehicle (n=20) and Test Item (n=20). Mice received 2 oral doses per day of **50 mg/Kg** of Test Item (100 mg/kg/day) during 28 days. This dose was selected based previous studies (efficacy and acute toxicity).

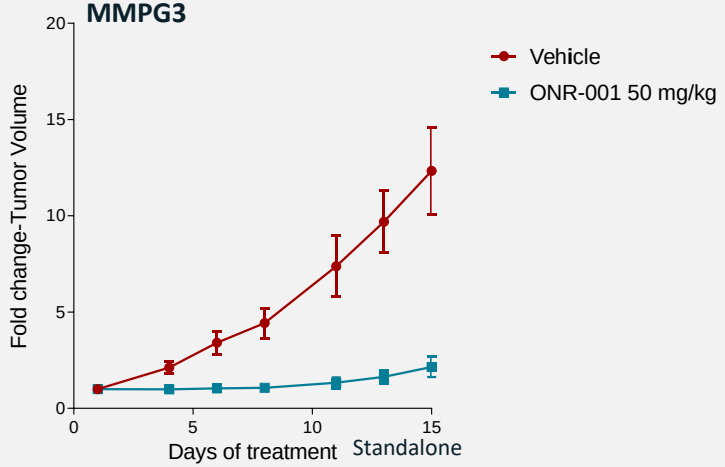
CONCLUSIONS

1. Clinical signs observed in both experimental groups: decreased motor activity, moderate piloerection, aggressiveness, hunched posture, mild dehydratation, body weight loss and changes in urine colour.
2. Biochemistry analysis: transaminase (ALT), aspartate transaminase (AST), creatinine, total protein and urea were within the physiological reference values.
3. Haematological analysis: all the results were within the physiological reference values.

EFFICACY & DIFFERENTIAL FEATURES FACING THE MARKET

ONR-001 is an effective small molecule *in vivo* alone or in combination in melanoma

Melanoma WT in orthotopic PDX animal model MMPG3

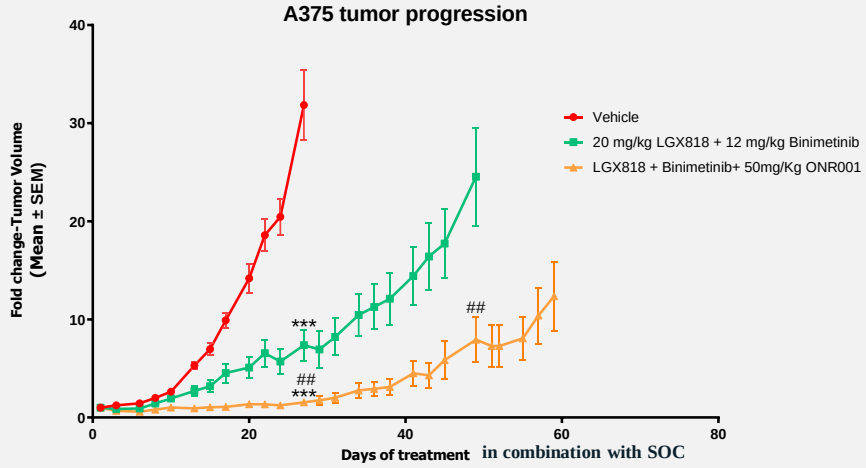


Treatment with ONR-001 in combination or at progression to immunotherapy will be evaluated

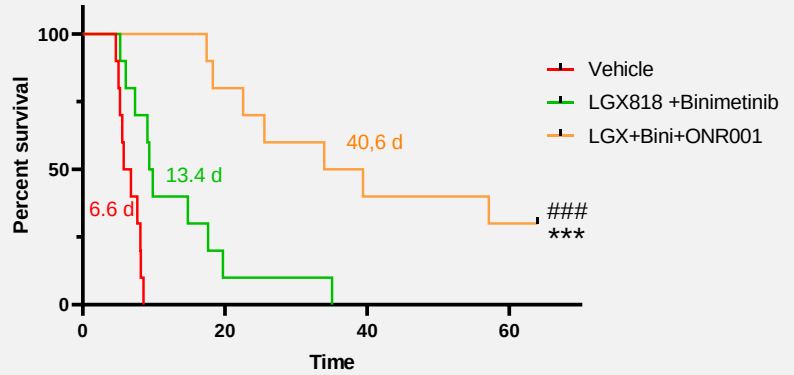
Treatment with ONR-001 in combination or standalone are being evaluated in other orthotopic / heterotopic animal models of other indications, such as AML or CRC

Melanoma BRAF^{V600E}mut in orthotopic animal model

A375 tumor progression

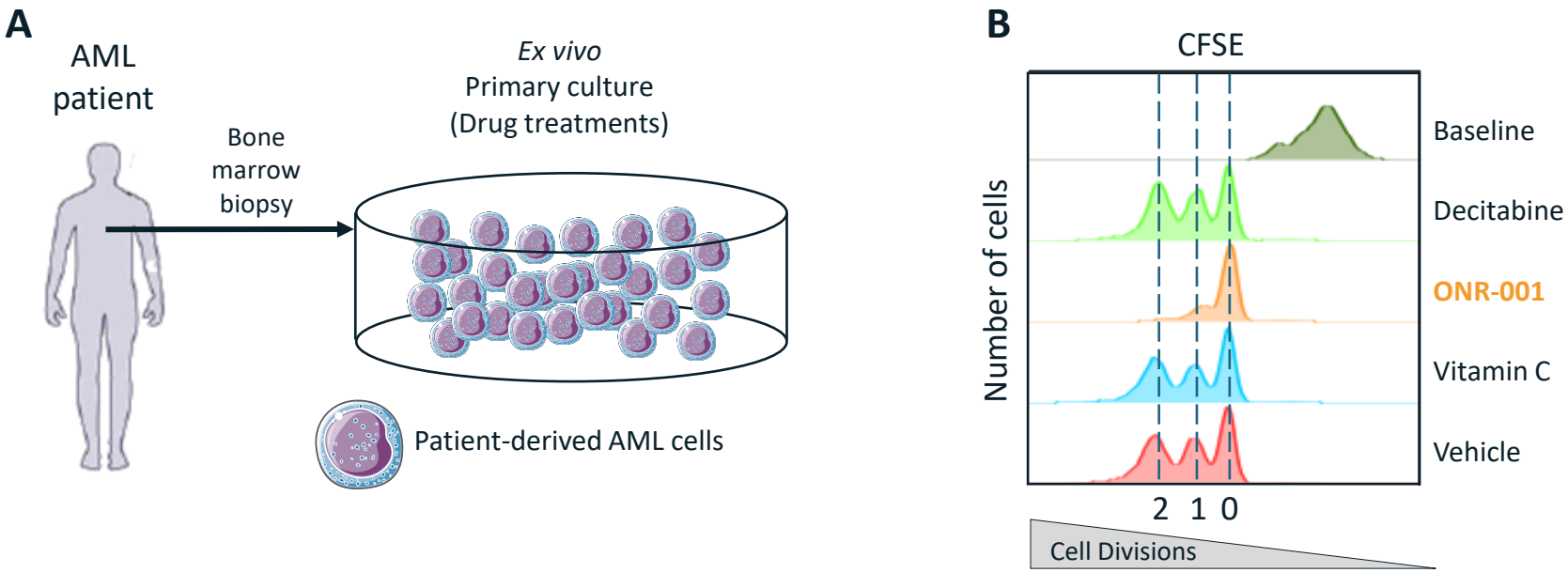


Progression-free survival A375 64 days



EFFICACY & DIFFERENTIAL FEATURES FACING THE MARKET

ONR-001 blocks the proliferation of patient-derived AML cells

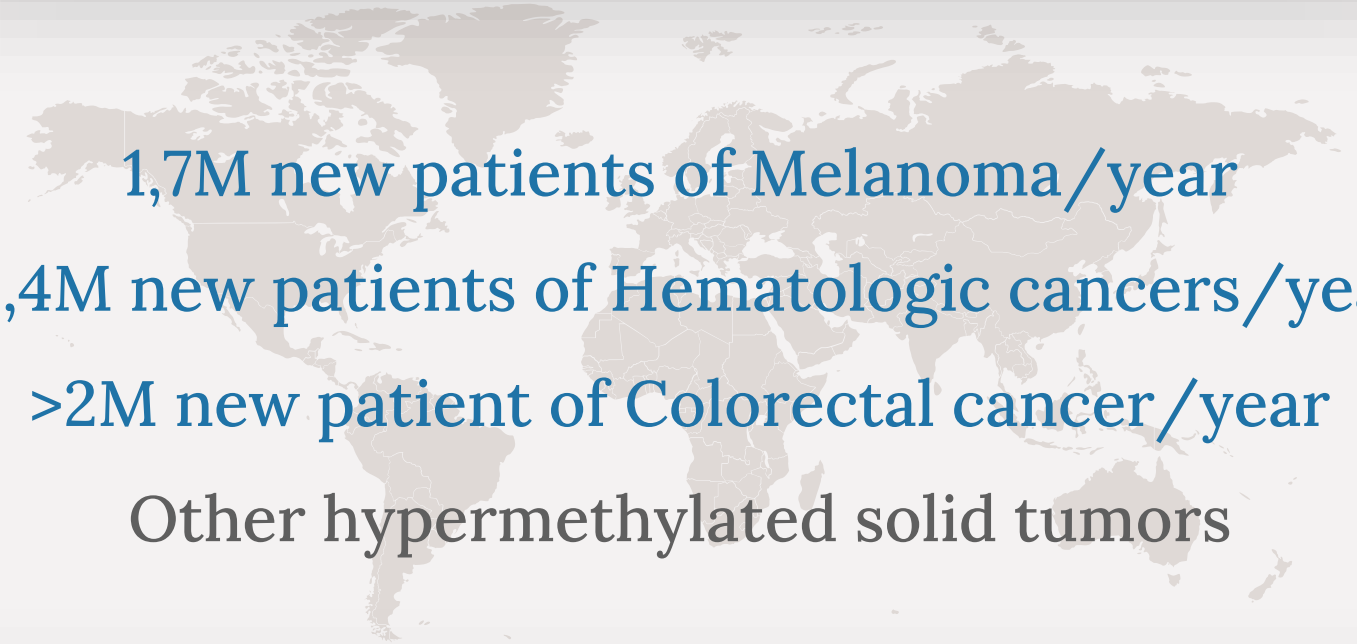


INDICATIONS & MARKET

ONR-001 is a Targeted Therapy whose Total Addressable Market reaches between 37% and 80% of the Total Market

>4,5M

Patients could be treated annually with ONR-001



1,7M new patients of Melanoma/year

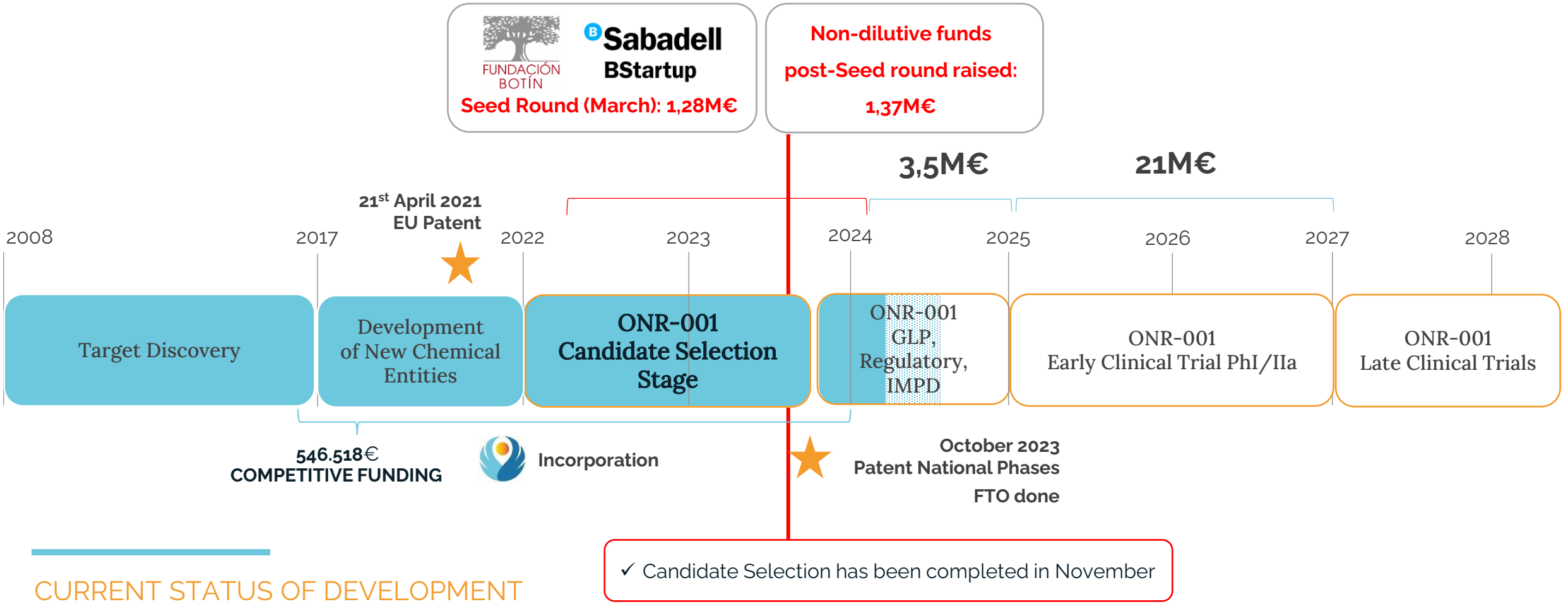
>1,4M new patients of Hematologic cancers/year

>2M new patient of Colorectal cancer/year

Other hypermethylated solid tumors

ONR-001

is indicated for TET2-dependent cancer



CURRENT STATUS OF DEVELOPMENT

Lead compound has been selected for entering pre-clinical regulatory phase

PIPELINE

PRODUCT	INDICATION	TARGET DISCOVERY	HIT-TO-LEAD	LEAD OPTIMIZATION	CANDIDATE SELECTION	PRE-CLINICAL REGULATORY	PHASE I/IIA	PHASE II	PHASE III	REGULATORY SUBMISSION	STATUS
ONR-001 TET2 ACTIVATOR	MELANOMA, CRC, AML & MDS.										CANDIDATE SELECTION & PRE-CLINICAL NON-REGULATORY STUDIES
ONR-002 TET2 INHIBITOR	ONCOLOGY										HIT-TO-LEAD
ONR-003 TET2 PROTAC	ONCOLOGY										HIT-TO-LEAD
NEW TARGETS	ONCOLOGY										DISCOVERY
ONR-004 TET2 ACTIVATOR	AGING			CO-DEVELOPMENT PROGRAM							CANDIDATE SELECTION & PRE-CLINICAL NON-REGULATORY STUDIES

PRODUCT	INDICATION	DISCOVERY	DEVELOPMENT	PRE-CLINICAL VALIDATION	CLINICAL VALIDATION & PRODUCT APPROVAL	PHASE III CLINICAL USE	MARKET USE	STATUS
BIOMARKER 5hmC	TET2 ACTIVATOR & INHIBITOR							DEVELOPMENT

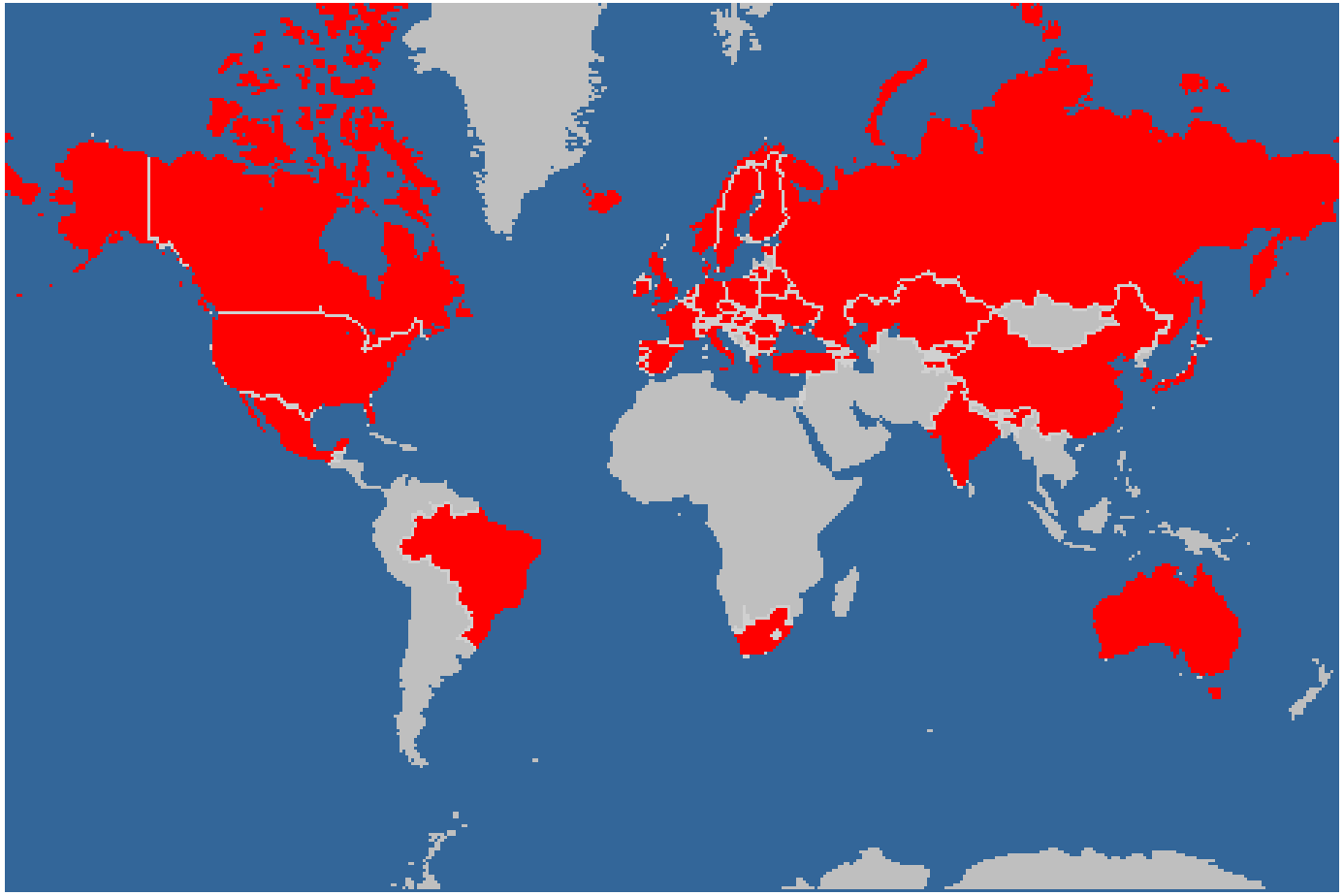
Current IPR Protection

ONR-001: Composition of matter patent

Currently in National Phases (Oct-2023) in the next countries: Australia, Brasil, Canada, China, South Corea, United States, Europe, India, Japan, México, Eurasia, Israel and South Africa.

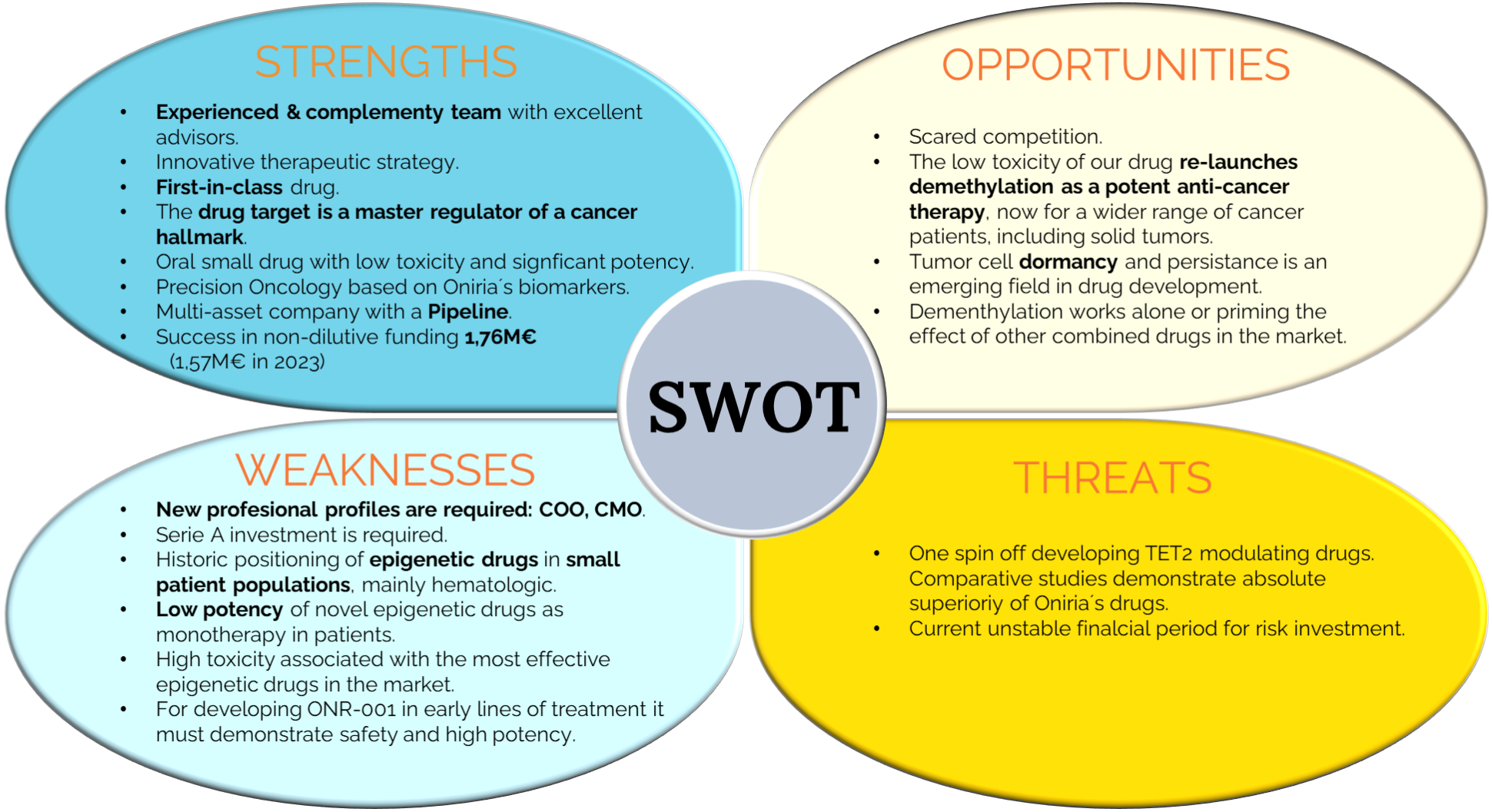
FTO done

Exclusive Worldwide license agreement



SWOT Analysis

The low toxicity of our drug re-launches demethylation as a potent anti-cancer therapy



Partnering Opportunities

Actively looking for Investment & Collaboration Agreements

Investment

Investment opportunity. We will be opening an investment round in February 2024.
Actively seeking an investment consortium including Venture Capital and Pharma firms.

Collaboration in Cancer

Collaboration opportunity/Co-development in Preclinical & PhI/IIa clinical stage.
Licensing-in opportunity in preclinical/clinical stage.

Collaboration beyond Cancer: Neurodegenerative-related diseases

Collaboration opportunity in Drug Discovery stage.
Actively looking for a collaboration with a Biotech/Pharma company to co-develop new IP in neurodegenerative-related diseases.

ONIRIA®

THERAPEUTICS

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