

XXIII Encuentro de Cooperación Farma-Biotech

28 de noviembre de 2023

NAX035: A Berberine derivative for the treatment of cancer



Dr. Carme Plasencia

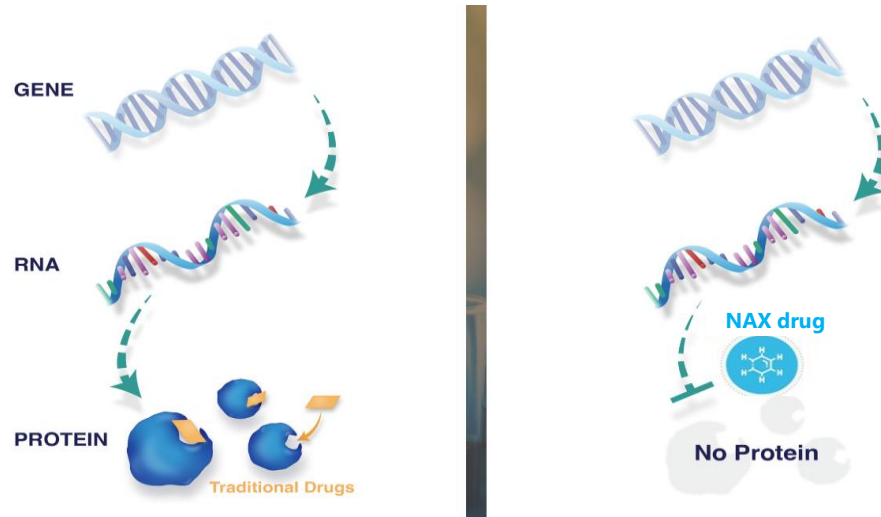


Content

1. Company overview
2. The concept behind
3. Product
 - a) Target Indication
 - b) Innovative mechanisms of action
 - c) Current status of development
 - d) Pitfalls & Risks to be considered
 - e) Differential features facing the market
4. Partnering Opportunities

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- › **Privately-held** drug development company mainly focused on Oncology
- › Developing a **novel class of RNA-targeting drugs**



- › Focusing on mRNA as therapeutic target
- › Addressing **targets with medical value** - oncogenic drivers whose overexpression are related to cancer progression and drug resistance
- › Addressing **poorly responsive tumors** and unmet oncology medical needs

- › A **first candidate** targeting TYMS-driven cancers advancing into Phase 1/2 trial
- › Further **pipeline expansion** into newer oncogenic targets

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Well-balanced and highly experienced management team

Dr. Carmen Plasencia Co-founder & CEO

- MBA, Ph.D. Medicine, BSc Chemistry
- 26years experience on oncology drug development
- 2 patents, Over 15publication
- EU external expert, Start-up mentor, BA



Mr. Narcís Clavell Co-founder, CFO & Chairman Board

- MBA (IESE), Telecommunications Engineer.
- Private investor of several SMEs in Europe.
- 30-plus years experience in moving academic technologies to commercial enterprises

International Advisory Board

Oncology drug development

 **Dr. Paolo Lombardi**
Naxospharma, CEO
R&D VP Chemistry Menarini,
Discovered Aromasin, for breast cancer

 **Dr. Cristina Geroni**
Aesis Therapeutics, CEO
35+yr Oncology R&D
Ex-Head Preclinical Nerviano.

 **Dr. Albert Abad**
Medical Oncologist
35+ yr Oncologist MD, PhD.
Head of the Digestive Unit Institut
Oncològic Dr. Rosell

Financial & business strategy

 **Dr. Werner Wolff**
Bioinnovation, CEO
VP of R&D at Boehringer Mannheim
Executive postictions TVM Capital

 **Dr. Nancy J Levy**
Biohealth Management CEO
CEO of Immunetics, together with
different executive positions at
Genzyme and Millennium.

 **Ms. Orily Pratt**
CEO Orily Pratt consultancy
Marketing, branding & positioning
+25 years experience in Marketing
in top global corporations

Key Support

curellsuñol
INTELLECTUAL PROPERTY ATTORNEYS

RCD **ROUSAUD
COSTAS
DURAN** SLP

TA **Asesores
Audidores**

NN **INNOQUA**
Toxicology Consultants

TFS HealthScience

ICO
Institut Català d'Oncologia

**Universität
Zürich**

BWH BRIGHAM AND
WOMEN'S HOSPITAL



anagram

Macosa-Astom
Asbestos Victims

ChemCon
Good Manufacturing Partner

HIT

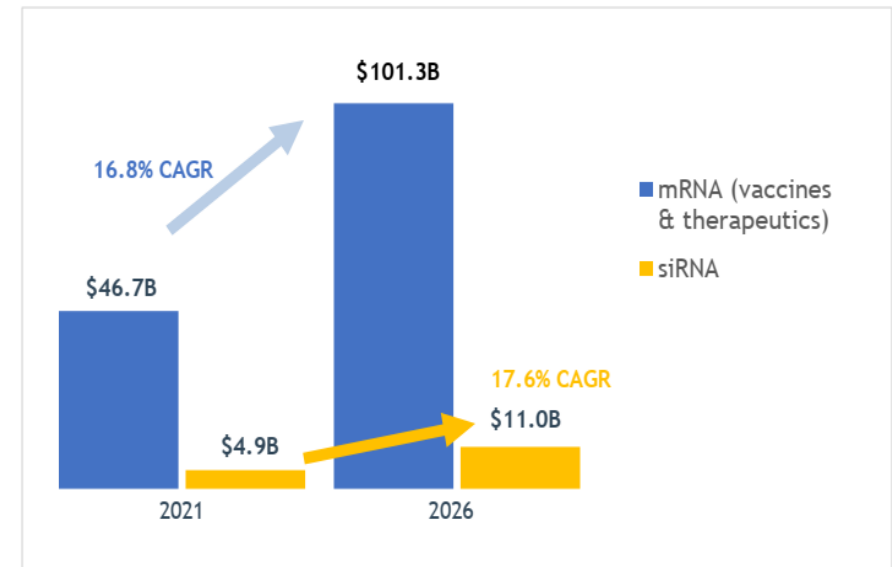
CHECKPOINT



Prasfarma

RNA THERAPEUTICS: Substantial market & growth opportunities

- RNA –therapies - A solution for “non-yet drugged” targets not amenable for therapeutic intervention
- RNA therapeutics Market is expected to reach \$1.2Bn (CAGR of 28,4%)
- Remarkable speed
 - mRNA vaccines have revolution the panorama
 - Recently approved mRNA therapeutics (2020) - RNA interference (siRNA, miRNA) and RNA antisense (ASO) are driving the market



Source: www.researchandmarkets.com; www.alliedmarketresearch.com

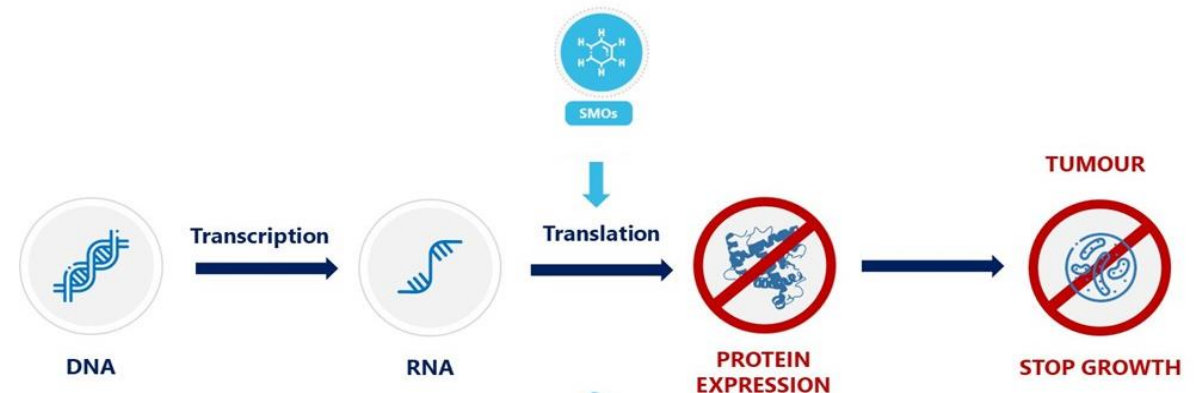
Oncology holds significant market share (40%) – next frontier growing market for mRNA therapeutics

SOLVING RNA THERAPEUTIC CHALLENGES

	RNA THERAPEUTICS		
	(RNA-binding small molecule)	ANTISENSE OLIGONUCLEOTIDES	RNAi (siRNA, shRNA, miRNA, mRNA)
TARGET SPECIFICITY	✓	✓	✓
ALL TARGETS	✓	✓	✓
LOCALIZATION (Intracel/Extracel.)	✓	✓	✓
POTENCY	✓	✓	✓
BIOAVAILABILITY	✓	✗	✗
LACK OF IMMUNOGENICITY	✓	✗	✗
STABILITY	✓	✗	✗
NO DELIVERY REQUIREMENT	✓	✗	✗
MANUFACTURE COST	✓	✗	✗
ORAL POSOLOGY POTENTIAL	✓	✗	✗

Our approach

By harnessing new insights into **mRNA structural domains**, AROMICS aims to develop newly **first-in-class molecules** targeting **translational control**, with **biological stability** and appropriate **pharmacokinetic** properties, that **selectively** bind to relevant transcripts involved in cancer and **silence nascent protein expression**











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SMALL MOLECULES TARGETING RNA _ A HOT TOPIC FOR PHARMA DEALS

Start up	Licensor	Indication	Date Deal	Terms (upfront + milestones)
Skyhawk Therapeutics	Celgene (BMS)	Autoimmune & metabolic diseases	26/06/2018	\$60M + Undisclosed milestones
Anima Biotech	Eli Lilly	Not disclosed	23/07/2019	\$30M + \$1.05B
Skyhawk Therapeutics	Biogen	Different indications including neurological	04/01/2019	\$74M + undisclosed milestones
Skyhawk Therapeutics	Celgene (BMS)	Autoimmune, oncology & immunoncology	12/11/2019	\$80M + undisclosed milestones
Skyhawk Therapeutics	Genentech	Cancer & neurodegenerative diseases	16/07/2019	Undisclosed upfront + \$2.0B
Skyhawk Therapeutics	Takeda	Neurodegenerative diseases	06/05/2019	Not disclosed
Skyhawk Therapeutics	Merck	Neurodegenerative diseases & cancer	12/05/2020	\$600M + milestones per program
Arrakis Therapeutics	Roche	Covering all Roche R&D areas	08/04/2020	\$190M + "several billion dollars"
Accent Therapeutic	AstraZeneca	Cancer & other diseases	04/06/2020	\$55M + \$1.1B
Skyhawk Therapeutics	Vertex	Not disclosed	22/12/2020	\$40M + \$2.2B
Ribometrix	Roche/Genentech	Not disclosed	06/01/2021	\$25M + \$1B
Rgenta Therapeutics	Lundbeck	Neurodegenerative diseases	01/08/2021	\$10M + \$100M
Arrakis Therapeutics	Janssen	Multiple therapeutic areas	01/01/2022	\$75 + "several billion dollars"
Remix Therapeutics	Janssen	Not disclosed	17/02/2022	\$45M + \$950M
Anima Biotech	Abbvie	Oncology	10/01/2023	\$42M + \$582M

AROMICS position in market –
Advancing our molecules to up to Clinical setting

SMALL MOLECULES TARGETING RNA	DISCOVERY	OPTIMIZATION	PRECLINICAL DATA	NON-CLINICAL PACKAGE	PRE-IND	CLINICAL
 SKYHAWK THERAPEUTICS						
 ARRAKIS THERAPEUTICS						
 ANIMA BIOTECH						
 EXPANSION THERAPEUTICS						
 ACCENT THERAPEUTICS						
 RIBOMETRIX						
 STORM THERAPEUTICS						
 AROMICS						

- > RNA targeting small molecules market ~ \$8.3 Bn in 2030
- > Two first FDA approved drugs (Duchenne and Spinal muscular atrophy). **None in oncology**

OUR TECHNOLOGY _ WHAT MAKES OUR **ASSETS UNIQUE**

An integrative technology platform combining best of cutting-edge anticancer strategies

1



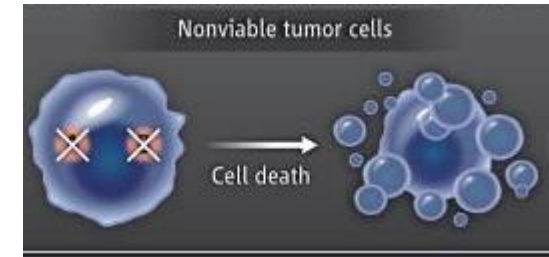
Small molecule targeting **specific regulatory elements** in mRNA of cancer targets

2



Chemical libraries of **bioactive ligands** affecting cancer cell metabolism

3



Expert knowledge to improve lead compound while looking for taking profit of **cancer cell vulnerabilities**

To create more effective Cancer Therapies for hard-to-treat oncology malignancies

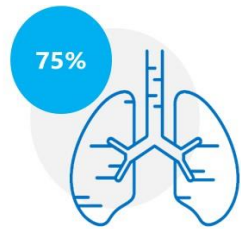
NAX035: Product Development

- **Strategic case indication PoC** – Malignant mesothelioma

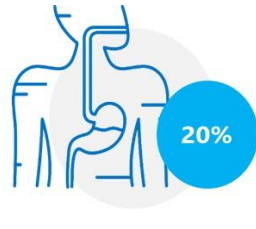


- **Scalability potential** in other indications

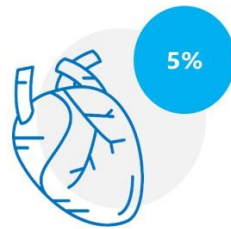
The medical need: Malignant mesothelioma - among the top ten occupational cancers of the world



**Pleural
Mesothelioma**
LUNGS



**Peritoneal
Mesothelioma**
ABDOMEN



**Pericardial
Mesothelioma**
HEART

A rare, aggressive and fatal cancer
9 to 12 months survival

Global Incidence

Mesothelioma is a rare form of cancer affecting people across all regions of the world.

North America
4,100

Europe
13,600

Asia
9,700

Central America
& the Caribbean
400

Africa
1,100

South America
800

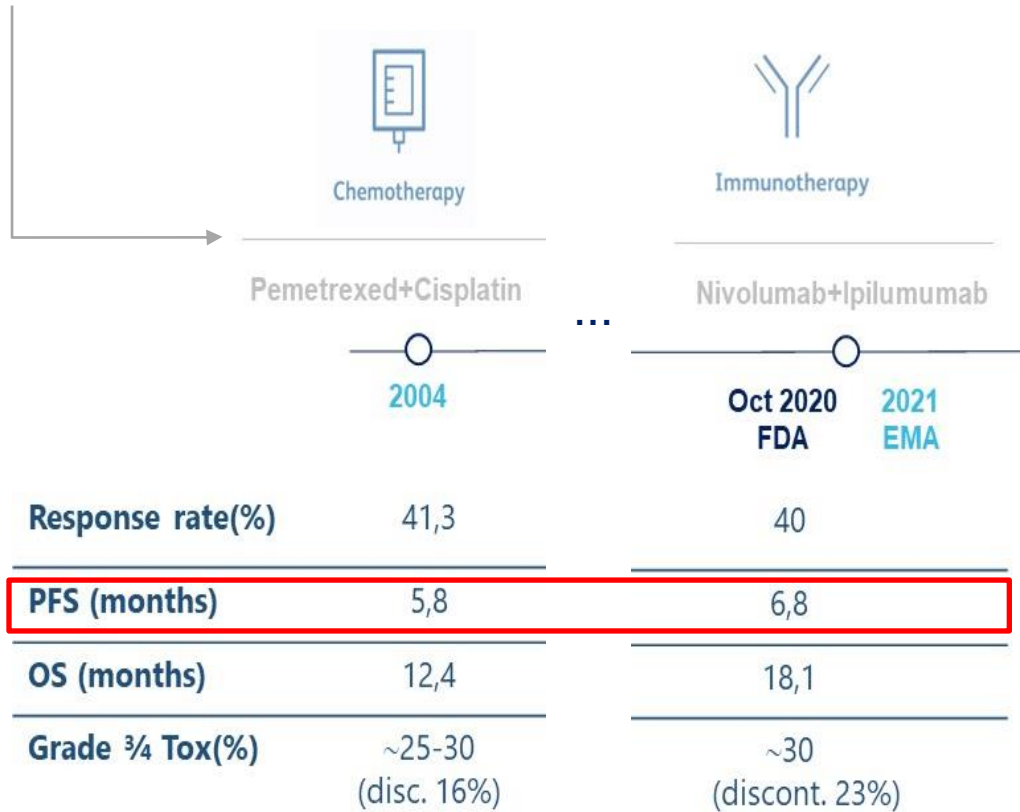
Oceania
1,000

Source: GLOBOCAN 2020

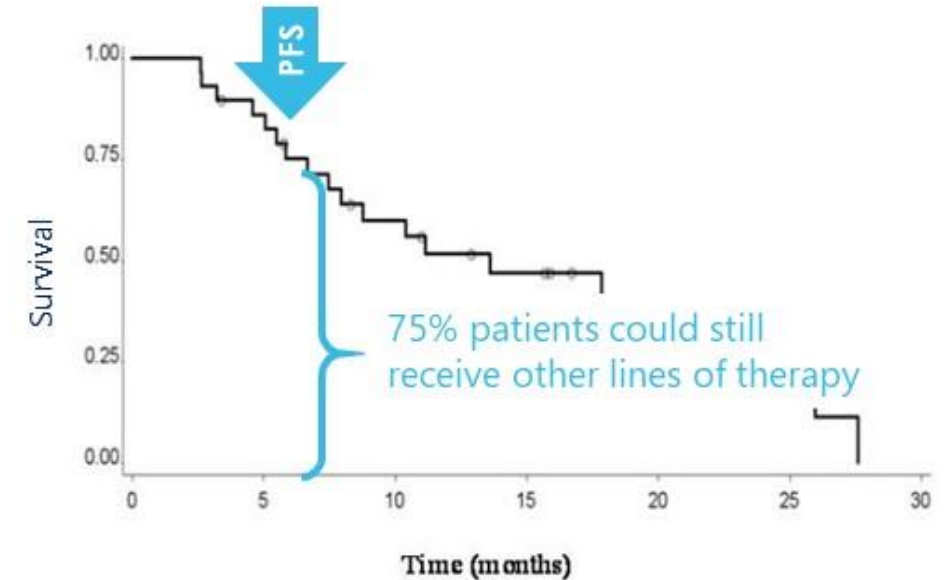
New cases per year are growing worldwide (CAGR 4,5%)

Despite intensive efforts, no good solution yet in market

90% Patients diagnosed at advanced stage



PFS: Progression-free survival; OS: overall survival



**Non-responders – No therapeutic option
Novel solutions are required**

Value proposition - binding to mRNA of a validated target in mesothelioma



De-risking development strategy

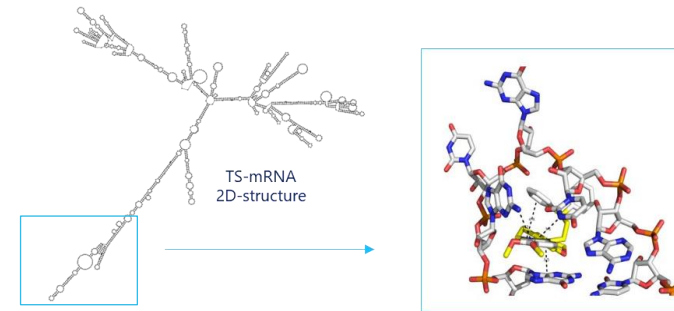
- › Clinically validated target
- › Rank among top 30 genes cancer cells needs for survive and growth (gene fitness score)
- › Involved in DNA replication and repair and Epithelial to mesenchymal (EMT) transition & metastasis



Predictive & prognostic value

- › Prognostic & predictive marker in solid & hematological tumors
- › TS overexpression correlates with poor prognosis and drug resistance
- › Antimetabolites & antifolates inhibiting TS protein are first-line cancer treatments

TS mRNA as therapeutic target



- › Identified a target element across TS mRNA
- › NAX035 compete with TS for binding to its cognate mRNA
- › Abolish aberrant protein expression
- › Post-transcription event – sustained silencing of TS protein without altering TS-mRNA expression level
- › Avoids primary or secondary-drug resistance due to TS protein overexpression



KOL support



Dr. Ernest Nadal

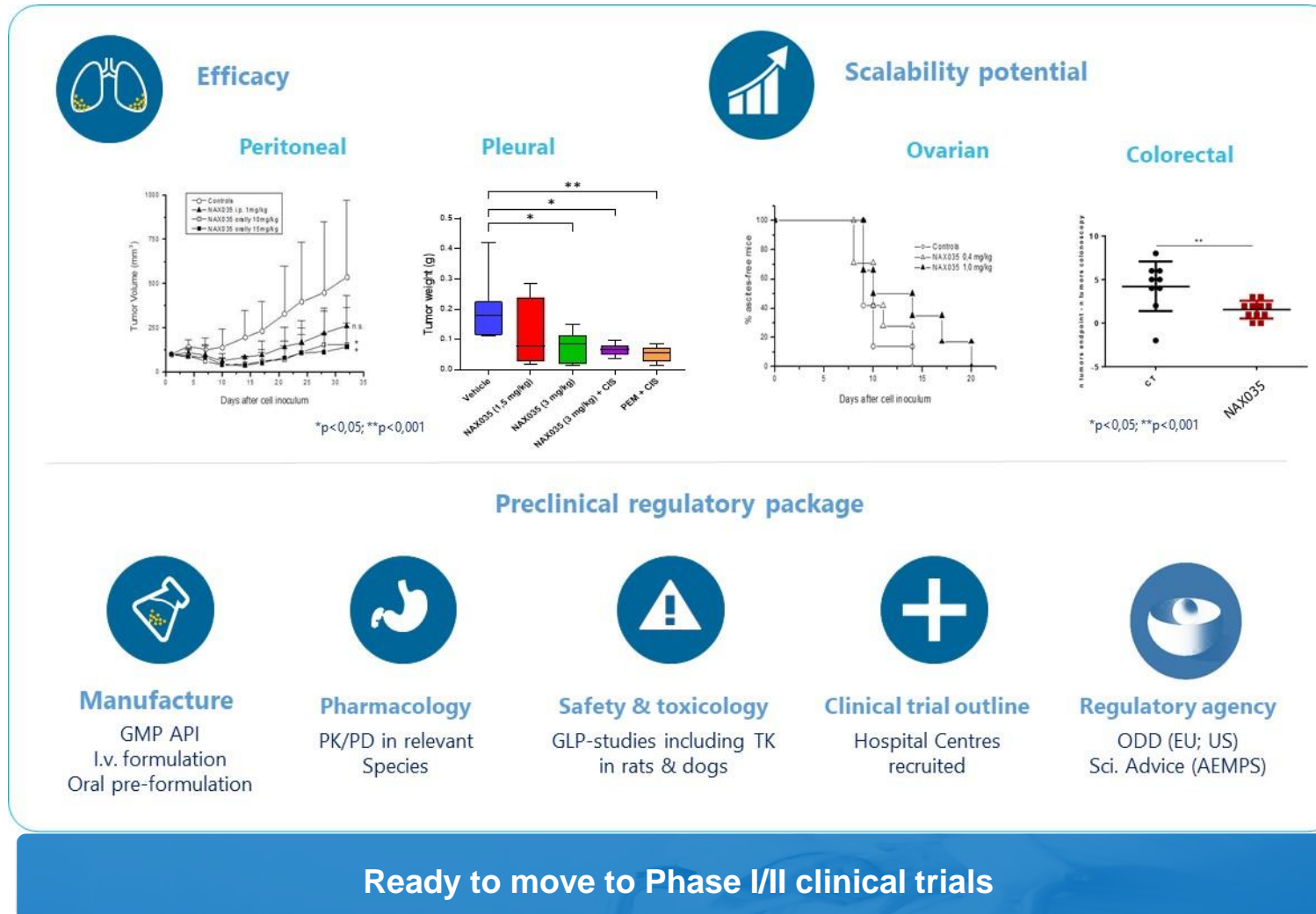


Dr. E. Felley-Bosco

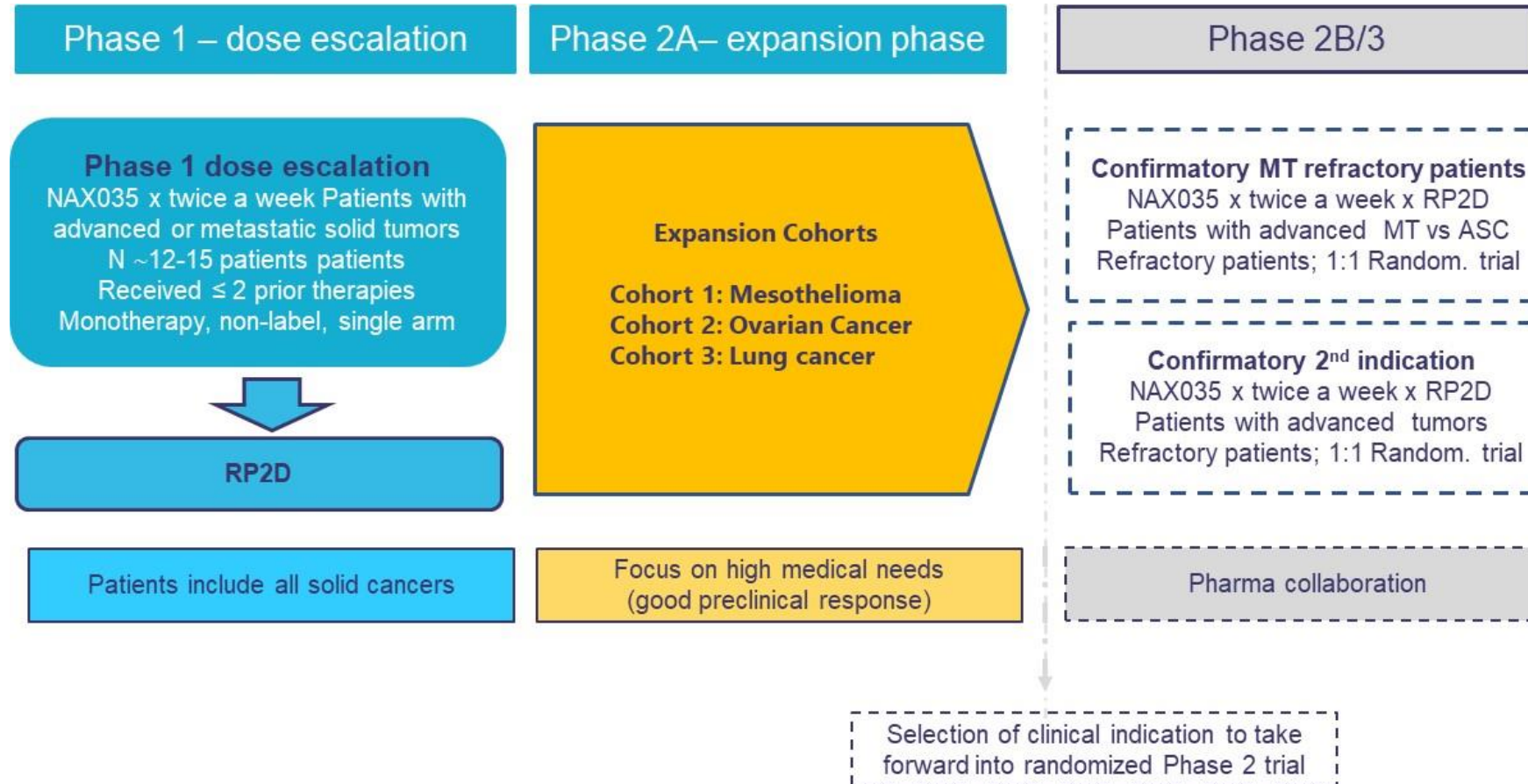


Dr. Raphael Bueno

NAX035- a highly valuable anticancer asset



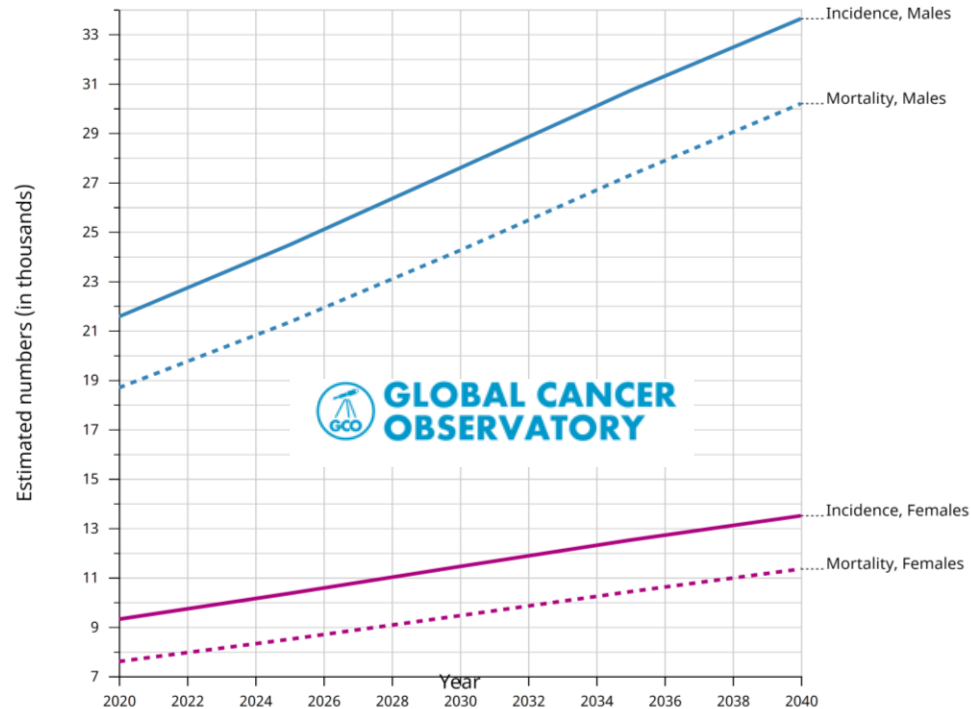
CURRENT DEVELOPMENT STATUS _ PHASE 1/2 CLINICAL DEVELOPMENT



Mesothelioma _ A Market opportunity ?

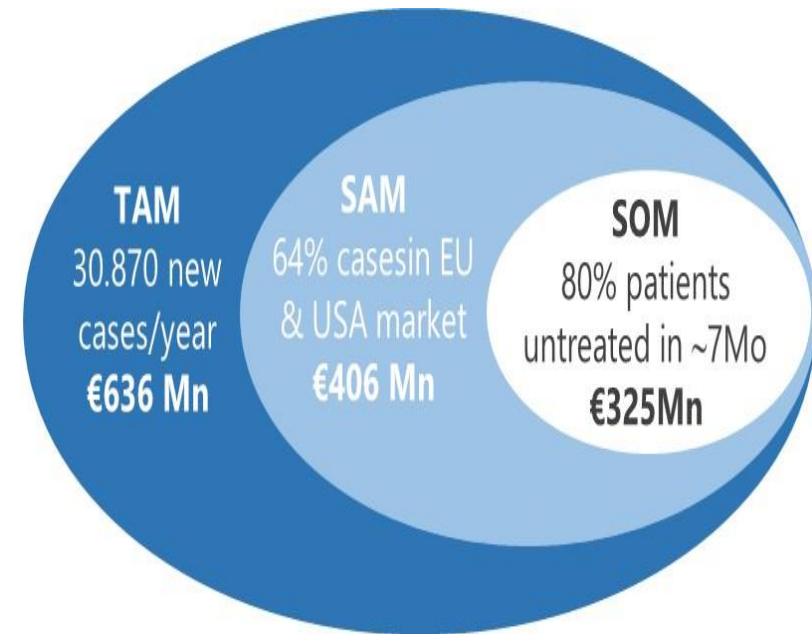
- Pemetrexed (standard of care) - patent loss
- Generics of Pemetrexed – same anticipated problems
- >75% patients – PFS in 6-7 months (even Immunoth.)
- **NEW therapeutic approaches** required for poor responders

Estimated world new cases from 2020 up to 2040

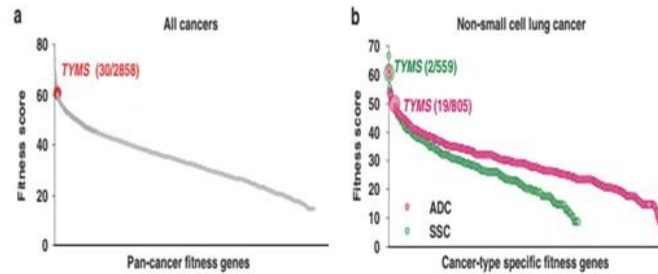


Cancer Tomorrow | IARC - All Rights Reserved 2023 - Data version: 2020

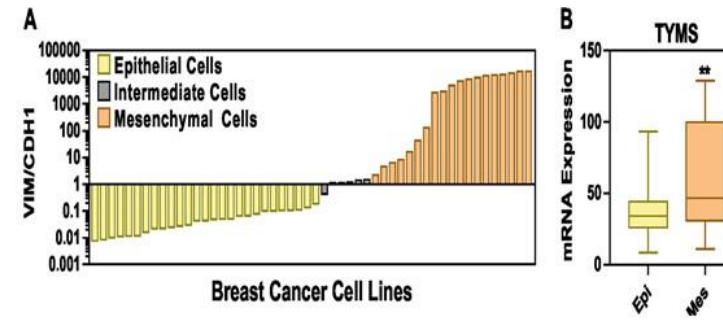
Market value \$636 Mn by 2025



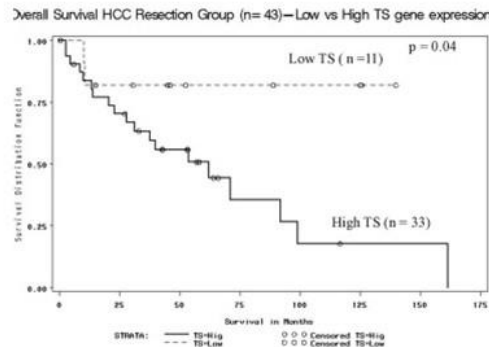
Targeting TS-mRNA, is highly relevant strategy in different tumors



TS is an essential NSCLC gene **TS in lung adenocarcinoma (ADC) and squamous cell carcinoma (SCC)**
Siddiqui A et al. *Br J Cancer* (2021) 124, 281–289

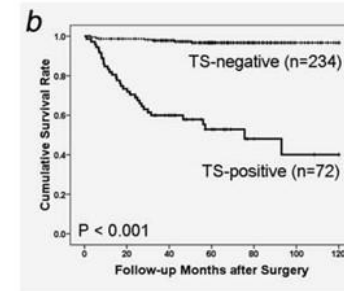


TS maintains the de-differentiated state of triple negative breast cancers
Siddiqui A et al (2019) *Cell Death Differ* 26, 2223–2236



TS prognostic and predictive marker after Hepatocarcinoma resection

Donner DB, et al.
PLoS One. 2019;14(7):e0219469.



TS predictive marker in pancreatic cancers. High levels prompts metastatic progression.

Lee et al, 2014, *Int. J. Cancer*: 135, 128–137
Kang M et al. *Cancer Lett*. 2018, 419:40-52

Overexpression of TYMS induced the development of tumors after a long latency, suggesting that aberrantly elevated TYMS cooperates with other cancer gene mutations to drive the neoplastic process

Potential market for additional indications



Squamous NSCLC



Ovarian cancer



Colorectal cancer



Pancreatic
cancer

What we offer in mesothelioma + further TYMS_driven tumors

Compared to	Main market attributes
Mesothelioma treatment	<ul style="list-style-type: none">› New Mechanism of action & patient selection› Enlarged market – combination with chemo/immunotherapy› Safety improvement› Targeting sensitive & refractory tumors, irrespective of histology
Classical TS inhibitors	<ul style="list-style-type: none">› First-in-class TS Translational regulator (silencing TS not inhibiting)› Engaging different anticancer response› Interfering on canonical and non-canonical activities of TS› Efficacy regardless TYMS expression levels
Other RNA-targeting compounds	<ul style="list-style-type: none">› Target specific -Proved ability as RNA ligand› Appropriate Efficacy PK, safety and tox› Non-immunogenic, no delivery requirement, good stability› Robust manufacture› Oral potential

NO SIMILAR PRODUCT IN MARKET – ADDRESSING TYMS-DRIVEN TUMORS

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Benefits of partnership With us

Strenghts of the compound	Benefit	Partner Benefit
Known target	First-in-class	De-risk clinical trial
Orphan indication	Lower n° patients & development costs	Market exclusivity
Clinical Trial	Additional TYMS-driven tumors	De-risk trial while scale-up
Regulatory challenges	Regular small molecule	Clear regulatory path
Financial requirements	Grant for phase 1 trial	Sharing development costs

Pitfalls & RISKS

RISK	Mitigation
Granted IP – composition of matter become old	<ul style="list-style-type: none"> > IP strategy > Ensured FTO > Orphan drug designation pursued
Strategy to market	<ul style="list-style-type: none"> > Development to market guided by indication > Precision medicine strategies > Looking for optimal combinotherapies
Irruption of other agents in mesothelioma market	<ul style="list-style-type: none"> > Orphan designation sought > Precision medicine strategies – selecting subset of patients with molecular characteristics

“Working on Innovative First-in-Class Therapies, Selectively Targeting RNA to Treat Cancer”

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