19 de noviembre de 2025

Ohmline therapeutic nanocarrier for treatment of metastatic cancer

Lifesome THERAPEUTICS

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AGENCIA ESTATAL DE INVESTIGACIÓN

MEDICAMENTOS INNOVADORES
Plataforma Tecnológica Española

farmaindustria

Content

1. Lifesome Therapeutics: company profile.
2. Ohmline Therapeutic nanoparticle for drug delivery
    a) Main Indication: castration resistant prostate cancer.
    b) Innovative mechanisms of action: tumor growth inhibition by synergic combination with docetaxel.
    c) Differential features facing the market: novel drug delivery. technology with intrinsic therapeutic capabilities.
    d) Current status of development.
    e) IPR protection.
3. Partnering Opportunities
    a) Pitfalls & Risks to be considered

1 - Company profile.

- **Biotechnology company developing lipid technology** for the creation of carriers focusing on oncology, vaccines, antimicrobial agents, and gene therapy.
- **Over 20 years of expertise,** guided by scientists: Jean-Marie Ruysschaert (COO), Christophe Vandier (CTO), and Ana Bouchet (CEO).
- **Multidisciplinary team with a global footprint.** Comprising 8 scientists with diverse expertise in fields such as biophysics, microbiology, and oncology.
- **Creators of Ohmline,** a unique therapeutic carrier in the market with versatile applications, capable of adapting to any treatment and drug. Proven efficacy through preclinical studies. Exclusive proprietary patent.

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XXVI Encuentro de Cooperación Farma-Biotech

JEAN-MARIE RUYSSCHAERT, PhD

Co-founder and COO

Liposome chemistry

CHRISTOPHE VANDIER, PhD

Co-founder and CTO

Ion channels electrophysioloy

ANA BOUCHET, PhD

Co-founder and CEO

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Torres Quevedo Senior Research Scientist

Preclinical and Regulatory Manager

DIEGO PAZOS, PhD

Torres Quevedo Senior Research Scientist

Oncology and Immunology

NATALIA ALFARO, PhD

Research Scientist

Microbiology

DIANA MARCOS

Research Scientist

Microfluidics formulations

INES OLIVER

Comunidad de Madrid Research Scientist

Industrial PhD – Glioblastoma

ADVISORS: Julio Martin, PhD. Life Science, **Prof. Thierry Lecomte,** MD., PhD. Oncology & **Paul-Alain Jaffrés**, PhD. Health and Materials

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Our differentials. Partners & collaborators

ULB Université Libre de Bruxelles

université de Tours

CONICET

Max-Planck-Institut für Polymerforschung
Max Planck Institute for Polymer Research

institute IMDEA food

CNB Centro Nacional de Biotecnología CSIC

UNI GRAZ

Bac³Gel
Unblocking the Full Power of Microbiota

CHRU Hôpitaux de Tours

IIS FJD Instituto de Investigación Sanitaria Fundación Jiménez Díaz

núbica CONSULTORIA I+D+i

Hospital Universitario Puerta de Hierro Majadahonda

Instituto de Medicina Molecular | João Lobo Antunes

Nantes Université

UCAM Universidad

e>olution_ Innovation Forward

i+12 Instituto de Investigación Hospital 12 de Octubre

Universitas Complutensis Matritensis

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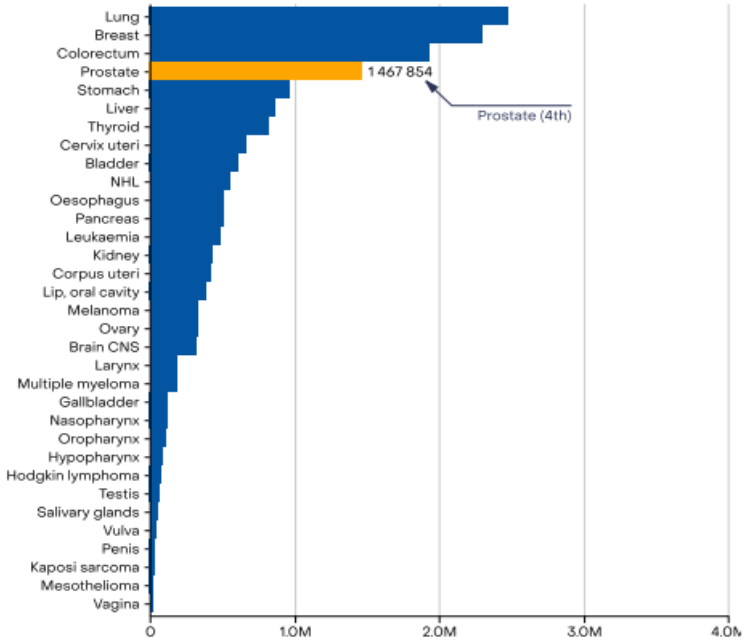
2a - Target Indication: Castration Resistant Prostate Cancer (CRPC)

Incidence

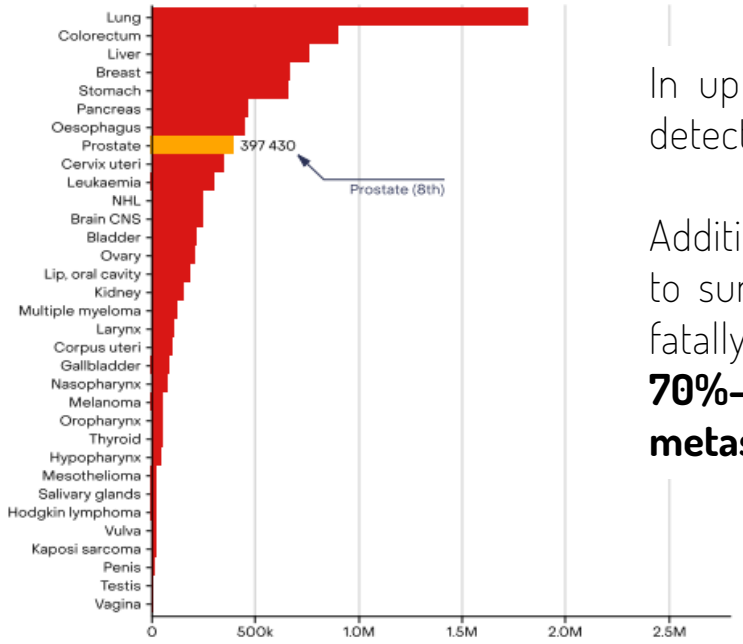
Rank	Cases	ASR (World)
4	1 467 854	29.4



Number of new cases , both sexes, all ages

Mortality

Rank	Deaths	ASR (World)
8	397 430	7.3



Number of deaths , both sexes, all ages

GLOBAL CANCER OBSERVATORY

International Agency for Research on Cancer

World Health Organization

In up to **10%** of patients **bone metastasis** are detected at initial diagnosis.

Additionally, **20%–30%** of the patients subjected to surgical removal of prostate will **relapse** and fatally progress to advanced disease, in which **70%–80%** of those patients will harbor **bone metastases**.

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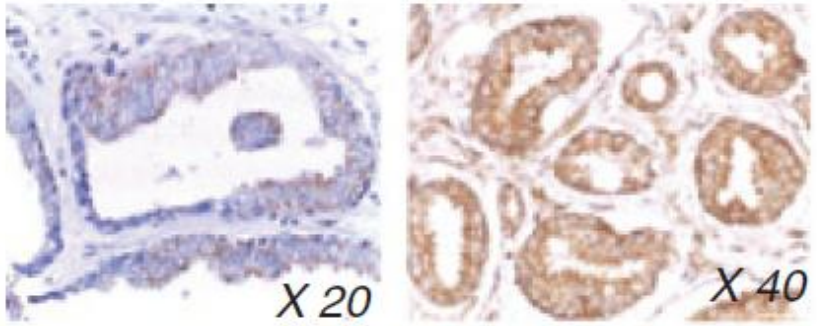
2a - Target Indication: Castration Resistant Prostate Cancer (CRPC)

- **Resistance** to Androgen Receptor **therapy** is common (around 30%) in prostate cancer.
- **SK3** (a potassium channel) is **overexpressed** in CRPC and plays a key role in tumor **cell resistance** to therapy.
- Vast majority (**80%**) of CRPC patients suffer **bone metastasis**. **SK3** plays a key role in bone metastasis in pre-clinical models.

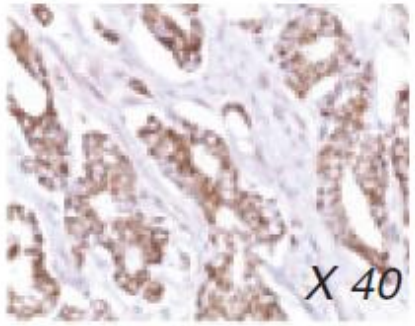
Primary Prostate Tumor



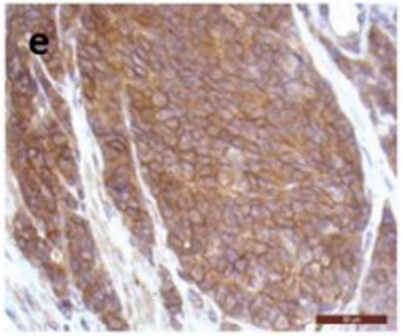
SK3 is expressed in 60% of primary prostate tumor simples (113 of 177) and bone metastases (9 of 15).

Chantôme et al., Cancer Res 2013;73(15):4852-61

Bone Metastasis



CRPC Adenocarcinome



SK3 is overexpressed ($p<0,0001$) in a sample set of CRPC adenocarcinome (n = 50) versus CLC (n=220). SK3 is shown in Brown.

Bery et al., Cancers 2021, 13(12), 2947

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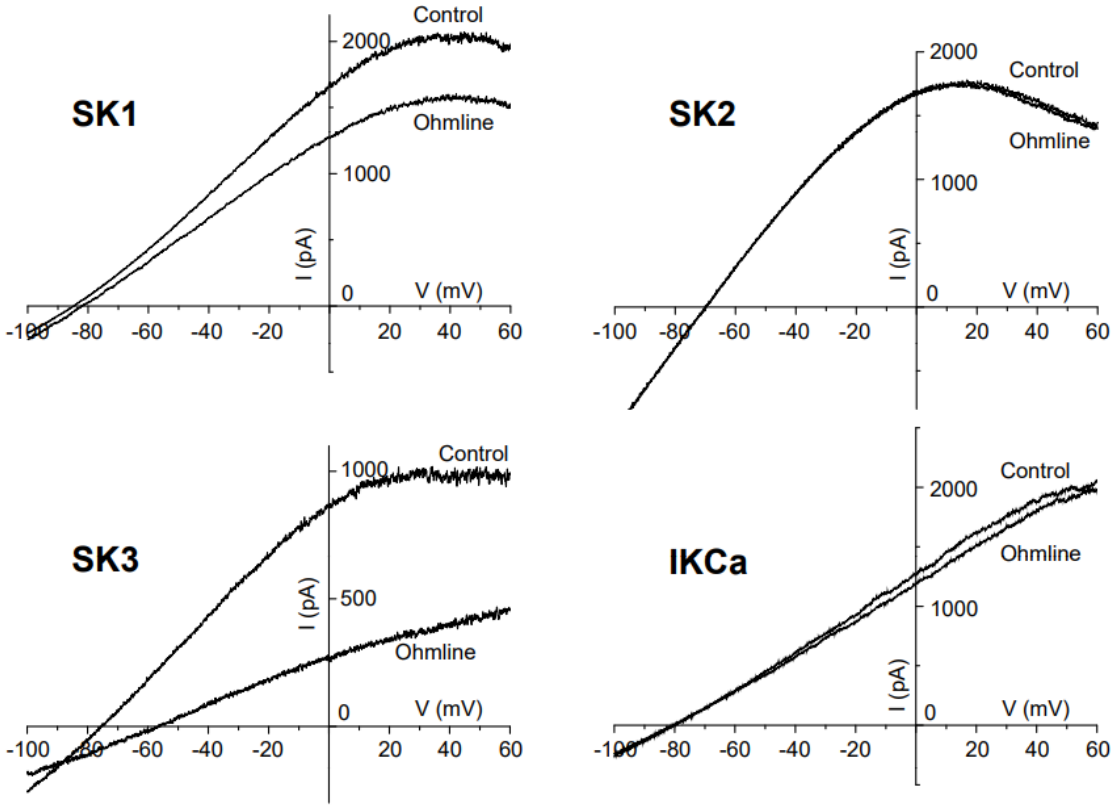
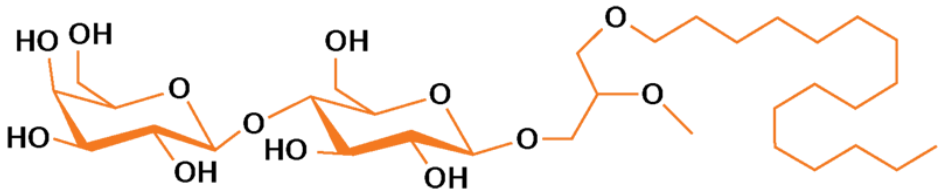
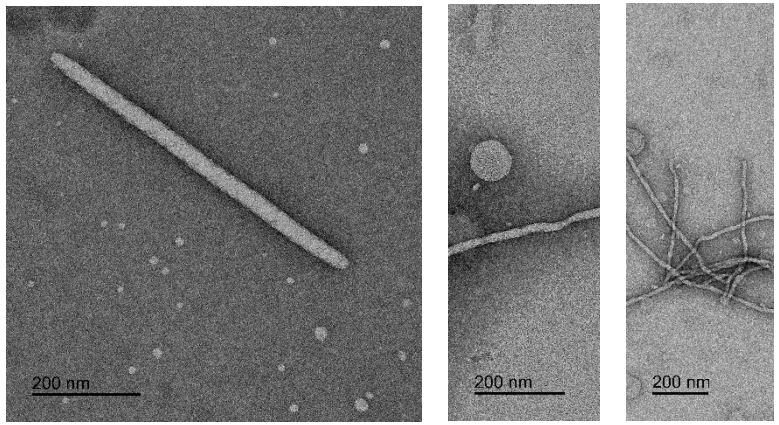
2a - Target Indication: Castration Resistant Prostate Cancer (CRPC)

- **Ohmline**, Lifesome's proprietary synthetic lipid, specifically **targets SK3** in tumors.
- **Ohmline** self-assembles in **nanoparticles and nanotubes**, working as a therapeutic **nanocarrier**.







Girault et al., Current Cancer Drug Targets, 2011, 11, 1111-1125

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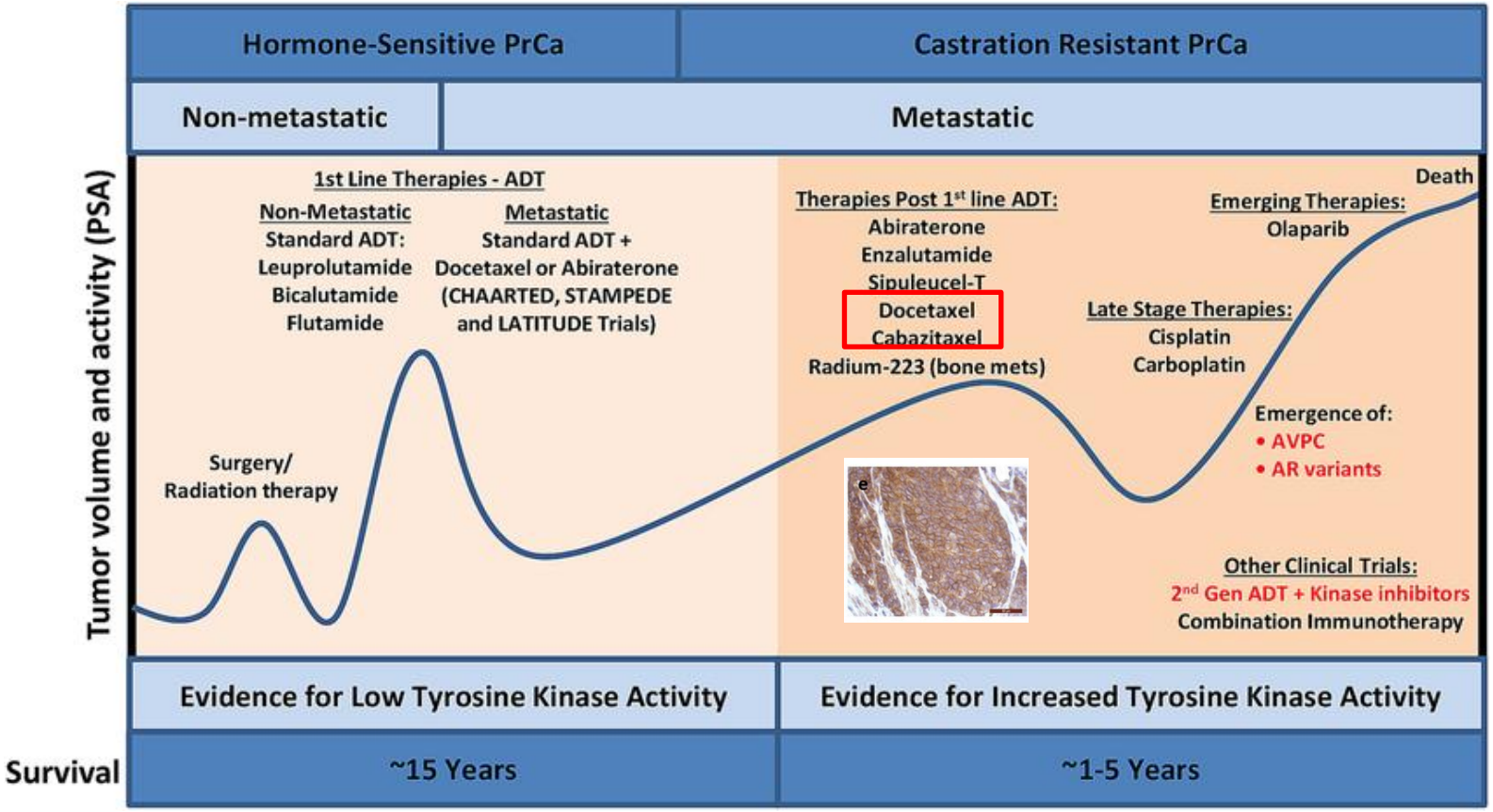
2a - Target Indication: Castration Resistant Prostate Cancer (CRPC)



- Only two palliative treatments for bone metastasis are available:
  Zoledronate (Bisphosphonate).
  Denozumab (anti-RANKL antibody).
- No significant improvement in life expectancy is provided by these drugs.
- **OHMLINE** might be **combined** with taxanes as a **second line therapy**, being expected an **increased** overall **survival** as a result of its **antimetastatic activity** through SK3 inhibition.

Ramroop JR, Stein MN and Drake JM (2018) Impact of Phosphoproteomics in the Era of Precision Medicine for Prostate Cancer. Front. Oncol. 8:28

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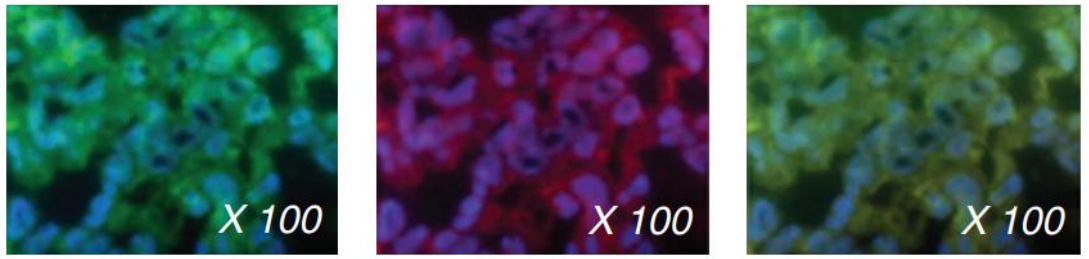
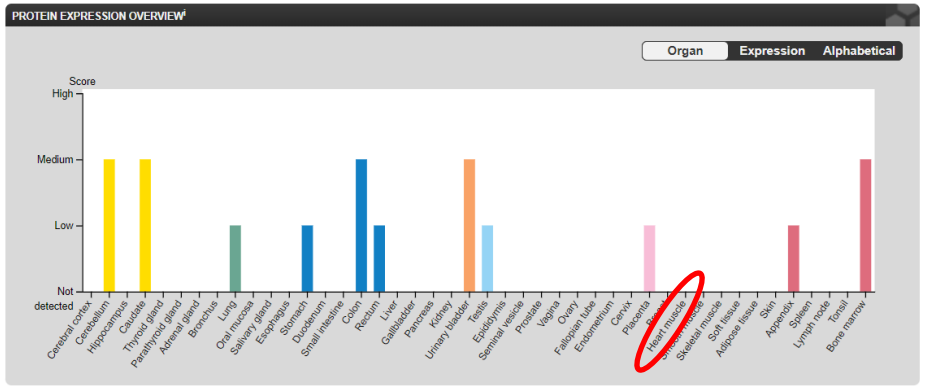
2b - Innovative Mechanism of Action: SK3 Ion Channel as a molecular target in CRPC

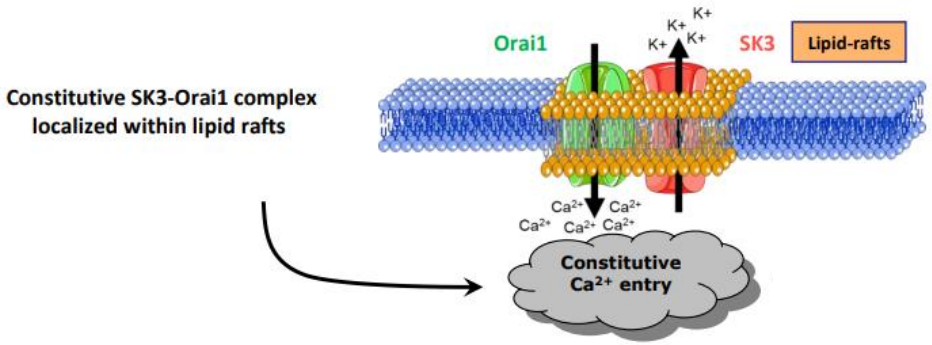
- SK3 protein is not expressed in most normal tissues. Thus, SK3 targeting should produce **low toxicity**.
- SK3 colocalize with Orai1 Calcium channel at lipid membrane lipid rafts in samples of prostate tumor.
- The channel complex **Orai1-SK3** mediates constitutive **calcium entry**.



Colocalization of SK3 (green) and Orai1 (red) at cell membrane of prostate tumor



The Human Protein Atlas



Chantôme et al., Cancer Res 2013;73(15):4852-61

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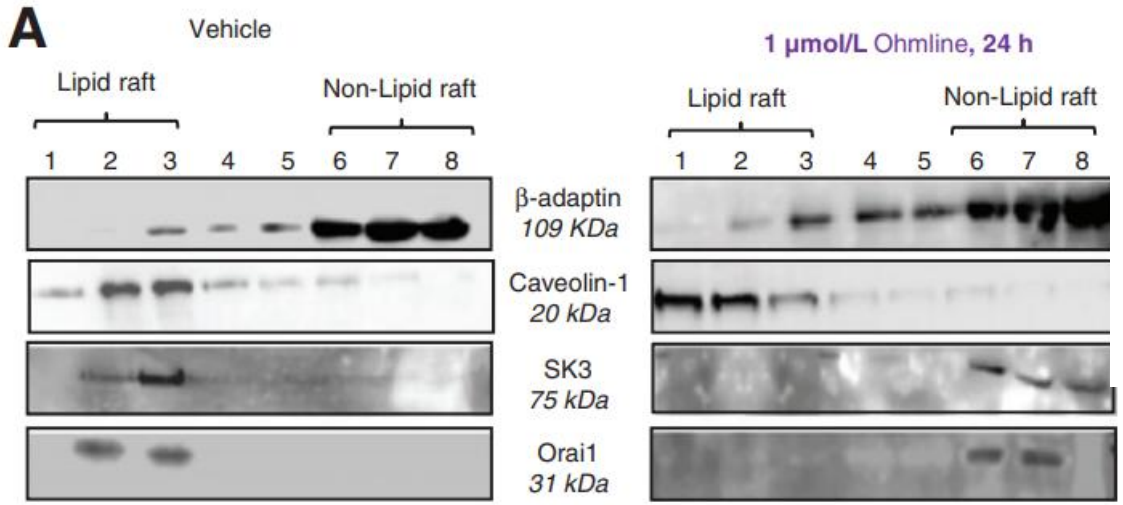
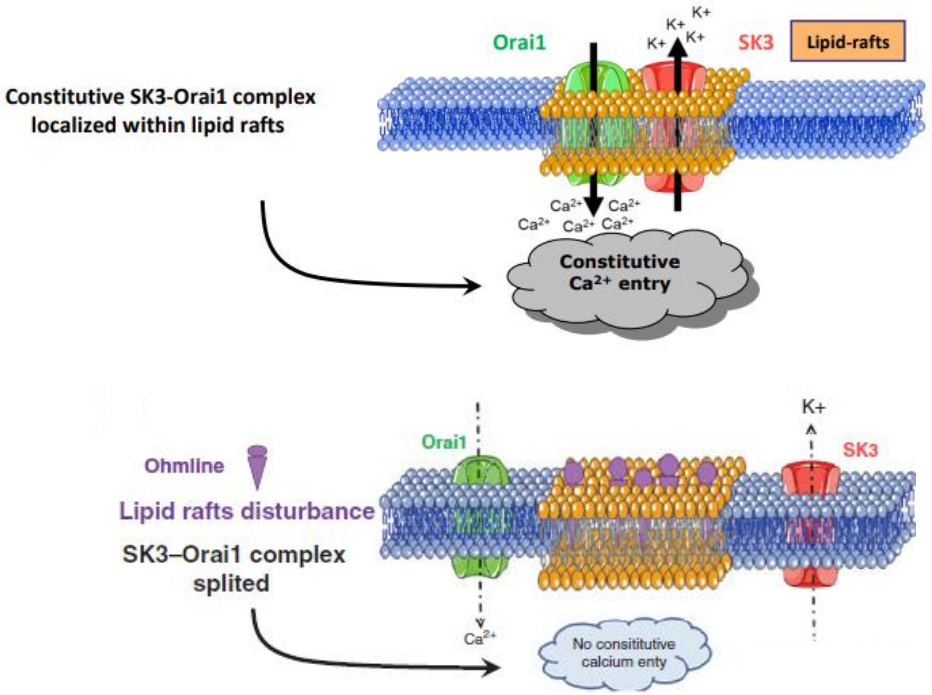
2b - Innovative Mechanism of Action: SK3 ion channel specific inhibition reduces intracellular Calcium.



Chantôme et al., Cancer Res 2013;73(15):4852-61



- OHMLINE expels SK3-Ora1 complexes from lipid rafts.
- As a result of SK3-Ora1 complex decoupling, cell **Calcium** levels are **decreased**.

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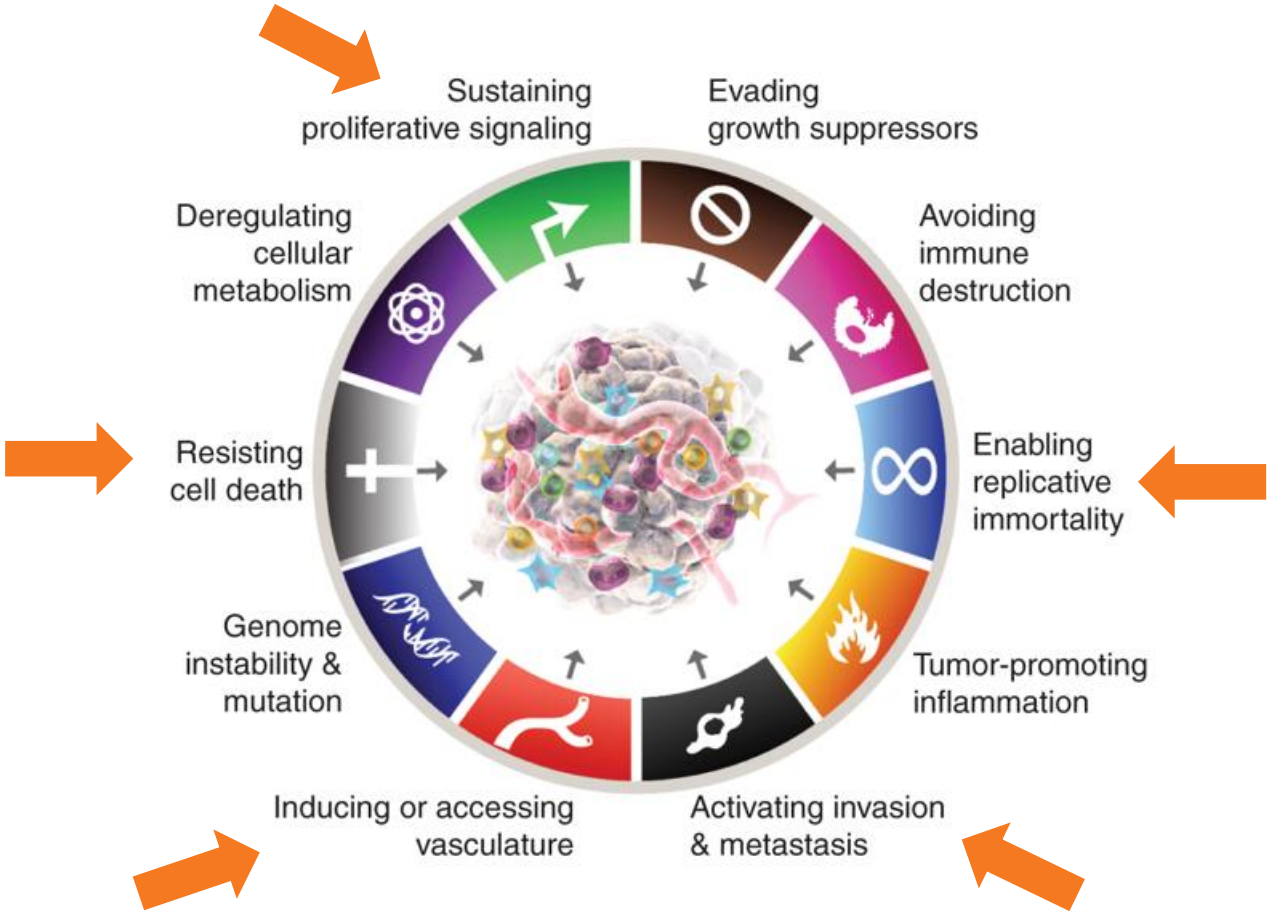
2b - Innovative Mechanism of Action: Calcium signalling disruption impacts major cancer cell processes.



Adapted from Hanahan et al., Cell, Vol. 100, 57-70, 2000

Increased intracelular Calcium exert cell effects:

- **Desregulation of cell cycle** leading to continuous cell proliferation.
- Inhibition of **pro-apototic mechanisms**.
- Activation of **angiogenesis** at tumor areas.
- Epithelial mesenchimal transition resultin in **cell migration** and **metastasis**.

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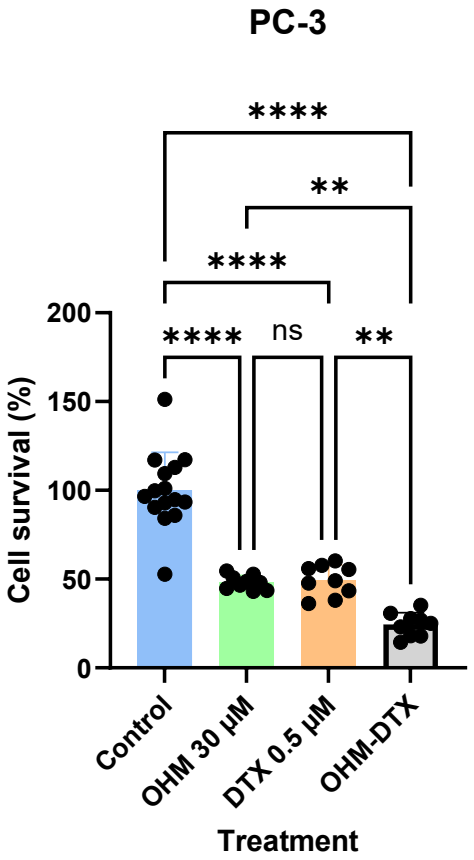
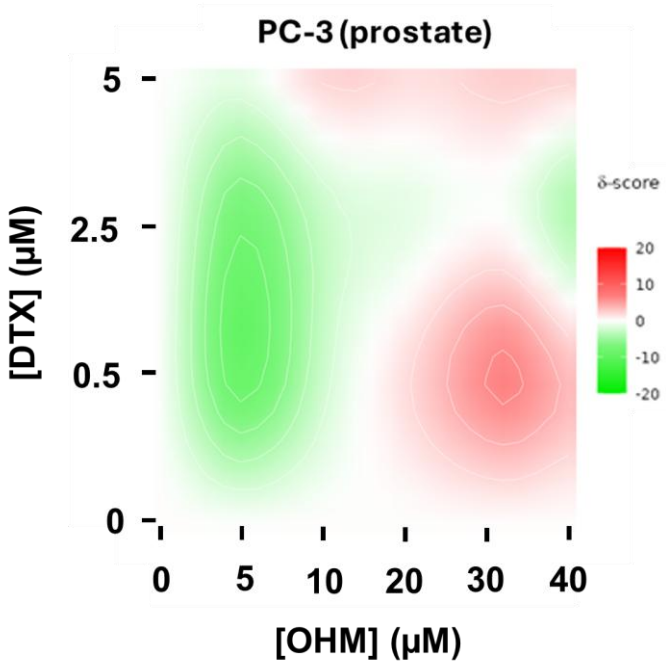
2b - Innovative Mechanism of Action: SK3 channel inhibition reduces PC3 cell proliferation in vitro.

IN VITRO

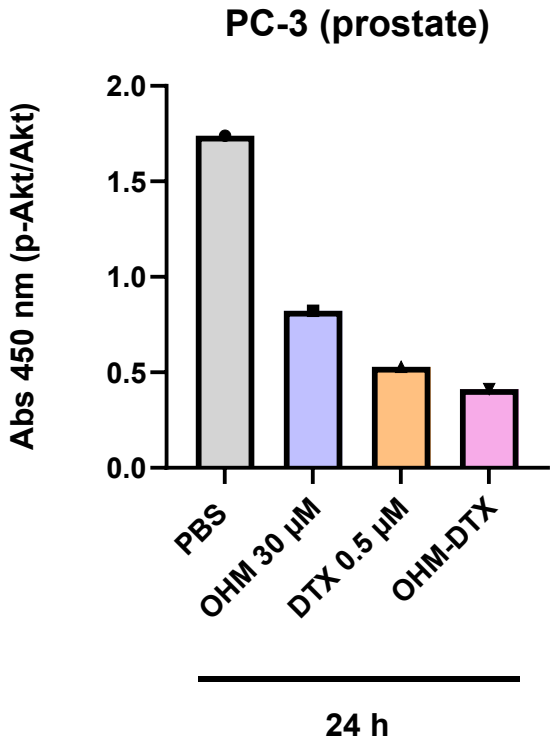


IN VITRO + IN SILICO ANALYSIS



RED: Synergy zone

IN VITRO



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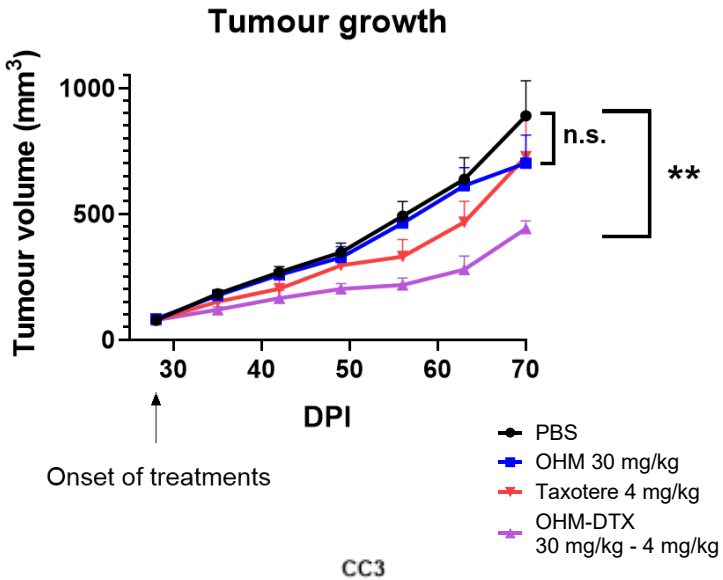
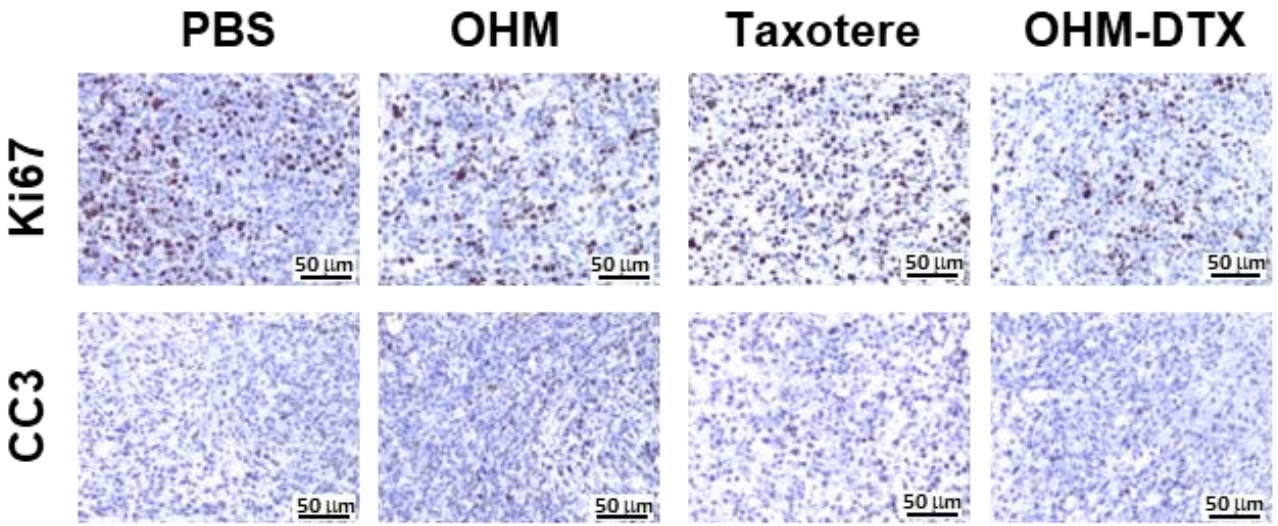
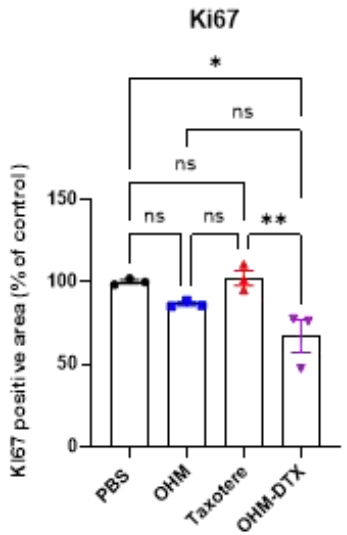
2b - Innovative Mechanism of Action: SK3 channel inhibition reduces tumor growth in vivo.

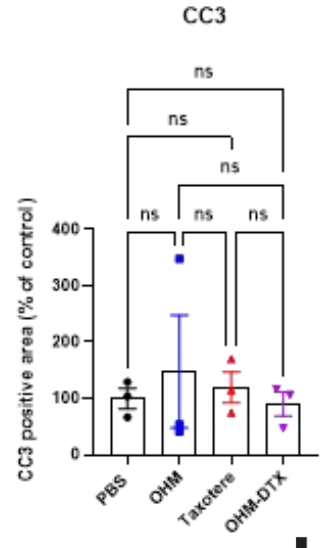
IN VIVO (PC-3 XENOGRAFT)

Treatments are administered by i.v. bolus once per week









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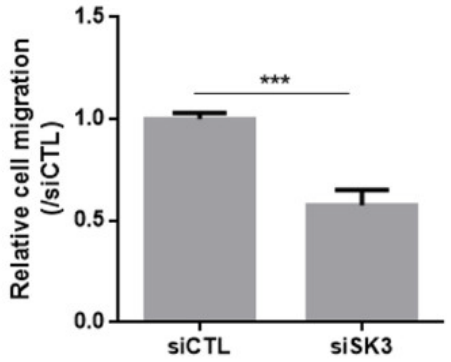
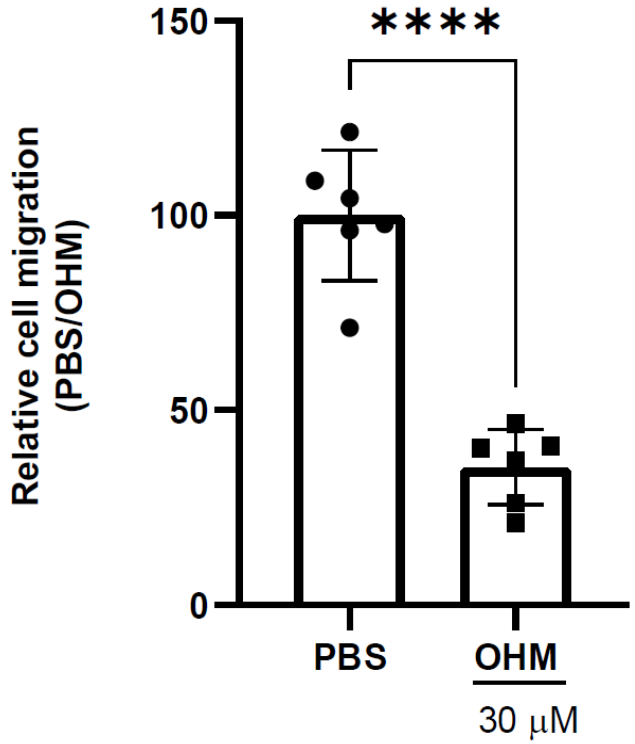
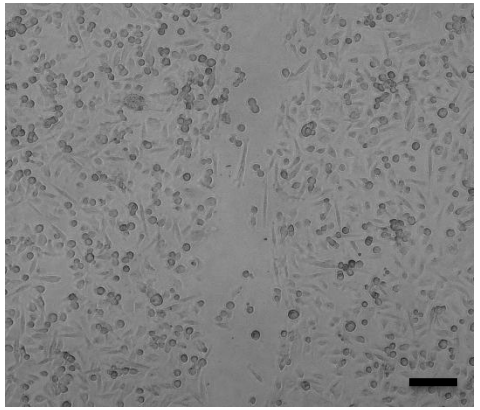
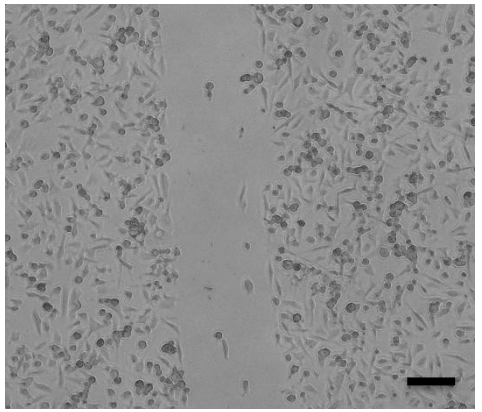
2b - Innovative Mechanism of Action: SK3 channel inhibition reduces PC-3 cell migration in vitro.







PBS
24 h



Ohmline 30 µM
24 h

Bery et al., Int. J. Mol. Sci. 2020, 21, 4786

PC-3 cell migration assayed in a wound healing model is significantly blocked when SK3 is both genetically and pharmacologically inhibited.

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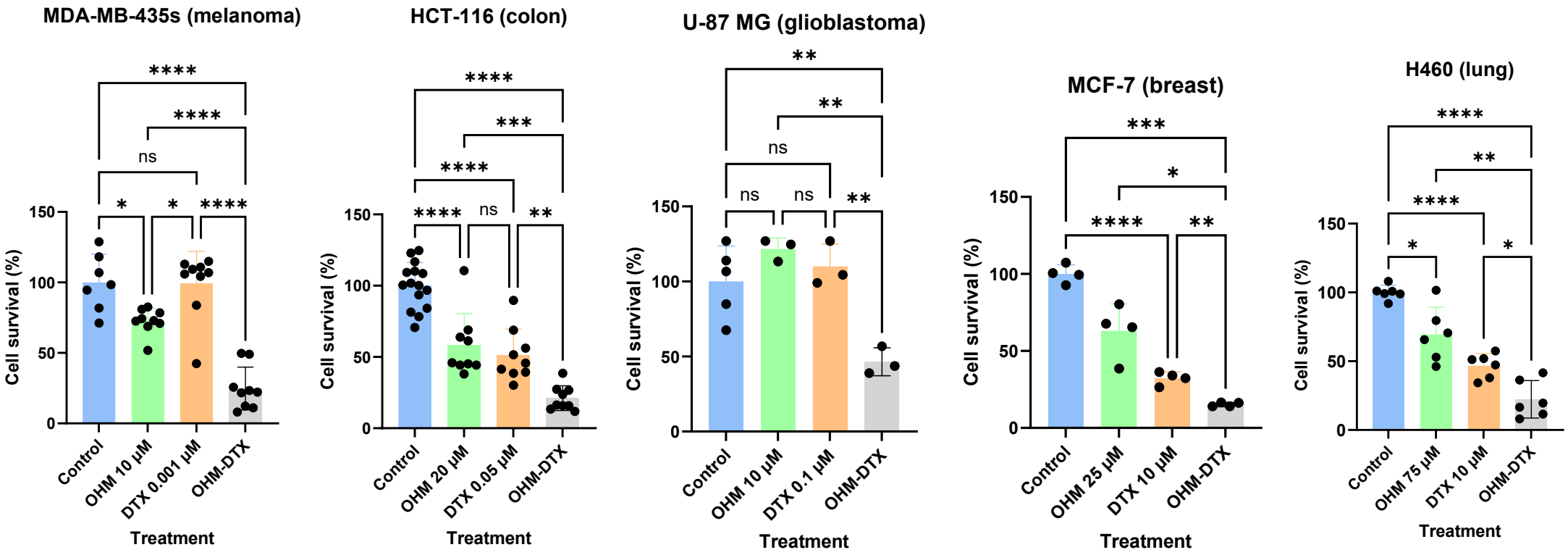
2b - Innovative Mechanism of Action: Ohmline reduces cancer cell proliferation in vitro in a wide range of cancer types.



2c - Ohmline differential features:

Ohmline holds all competitors features + Increased efficacy due to Ohmline's intrinsic activity

minimal differences in survival outcomes due to the absence of antitumoral activity of the nanoparticle

	Janssen Doxil (docetaxel) FDA 1995 EMA 1996	**BMS** Abraxane (paclitaxel) FDA 2005 EMA 2008	**JAZZ PHARMA** Vyxeos (daunorubicine + citarabine) FDA 2017 EMA 2018	**Celsion** Thermodox (doxorubicine) Phase III	**InnoMedica** Talidox (doxorubicine) Phase I/II	Lifesome THERAPEUTICS
Increased safety profile of the encapsulated therapy	✓	✓	✓	✓	✓	✓
Avoid large corona formation		✓			✓	✓
Encapsulation of 2 different drugs			✓			✓
Drug release in tumor environment				✓	✓	✓

No clinical trial can be found in development, on any indication, based on SK3 ion channel as a molecular target

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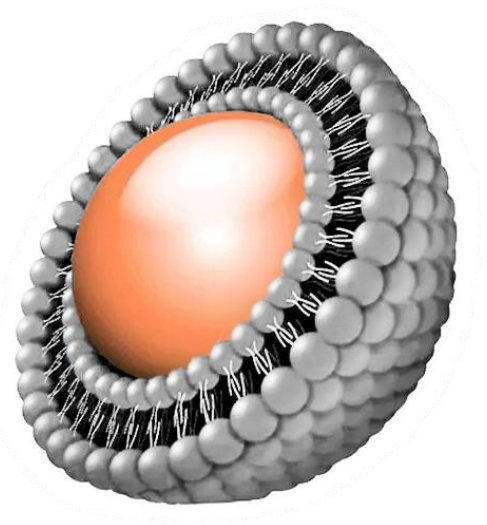
2c - Ohmline differential features: widely applicable to main healthcare areas.

ONCOLOGY

- Haematological cancers.
- Prostate cancer
- Breast cancer
- Lung cancer
- Colorectal cancer
- Urothelial
- Bone metastasis
- Melanoma
- Rhabdomyosarcoma

DISCOVERY

- Small molecules
- Protein therapeutics
- DNA, mRNA, siRNA therapeutics
- Antibiotic
- Immune therapeutics, immune modulation
- Vaccines
- Drug delivery solutions



HEALTHCARE SOLUTIONS FOR INTERVENTIONAL ONCOLOGY

- Innovative intratumoral therapies.
- Integrated delivery procedures for minimally invasive access.
- Innovative delivery systems.

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2d - Current Status of Development: preliminary pre-clinical testing.

2D Cell Migration Inhibition	PC3 cells non treated versus Ohmline 30 µM treated PC3 cells in a wound healing assay	non GLP	Cell migration is reduced in 30 µM Ohmline treated cells (60% inhibition)
SK3 Cell Migration Dependence	PC3 wild type cells versus PC3 SK3 defective (shRNA transfected)	non GLP	Cell migration is reduced in $SK3^-$cells (40% inhibition)
Patch Clamp HEK293 SK3 transfected	Whole cell potassium current recording along time upon treatment with Ohmline	non GLP	Dose response effect of Ohmline tested at 300 nM, 1 µM and 10 µM
Ohmline incorporation in tissues	Dosages intravenous (i.v.) consecutive 1 x 15 mg/kg, 3 x 15 mg/kg, 5 x 15 mg/kg.	non GLP	In the heart, brain and colon, the incorporation of Ohmline is directly related to the number of injections administered
Ohmline incorporation in tissues	Dosages(i.v.) of 2.5 mg/kg and 15 mg/kg, five days per week over a period of 2 weeks, concentration of Ohnmline measured by HPTLC	non GLP	Ohmline is still present in heart brain and lungs 4 weeks after end of administration.
Pharmacokinetics Oral Administration	Single dose of vehicle, 100, 200, 500 mg/kg Ohmline, High-Performance Thin-Layer Chromatography (HPTLC) detection	non GLP	No dose effect is observed. The concentration of Ohmline detected in bone tissues is four times greater than that observed in heart tissues
In vitro Cardiotoxicity	In vitro Ohmline binding to hERG channel, L Type Ca 2+ channel, Nav channel	non GLP	No significant binding below 2 µM Ohmline
GPCR inhibition	In vitro Ohmline binding to PAF receptor	non GLP	No significant binding below 2 µM Ohmline
Kinase inhibition	In vitro Ohmline binding to PKC	non GLP	No PKC activation in the range 1nM-10 µM Ohmline
Genotoxicity	In vitro bacterial reverse mutation test (Ames) and mammalian cell Micronuclei test	non GLP	No significant effect below 15 µM Ohmline
Oral route toxicity	Ohmline orally administered at 500, 100 and 10 mg/kg	non GLP	Good tolerance, no clinical sign (including behaviour), no mortality
Intravenous route toxicity	Ohmline administered 15 mg/kg, iv, 5 times/week for 2 weeks	non GLP	No apparent in vivo toxicity

- SK3 **Ohmline** inhibitor shows **no toxicity** as a **single agent** at non-GLP preliminary testing.
- **EMA**'s Innovation Task Force **supported** the **clinical development** of Ohmline-Docetaxel combination as a treatment for CRPC (meeting held on 16th December 2024).
- GMP batch in the process of being manufactured: final scale up in progress.
- Fund raising for externalising GLP PK/PD and toxicology studies in progress.

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2e - IP Protection: Two patents granted in major territories

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
25 August 2011 (25.08.2011)

PCT

(10) International Publication Number
WO 2011/101408 A1

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A61K 31/702 (2006.01) *A61P 35/04* (2006.01)

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17 February 2011 (17.02.2011)

(25) Filing Language: English

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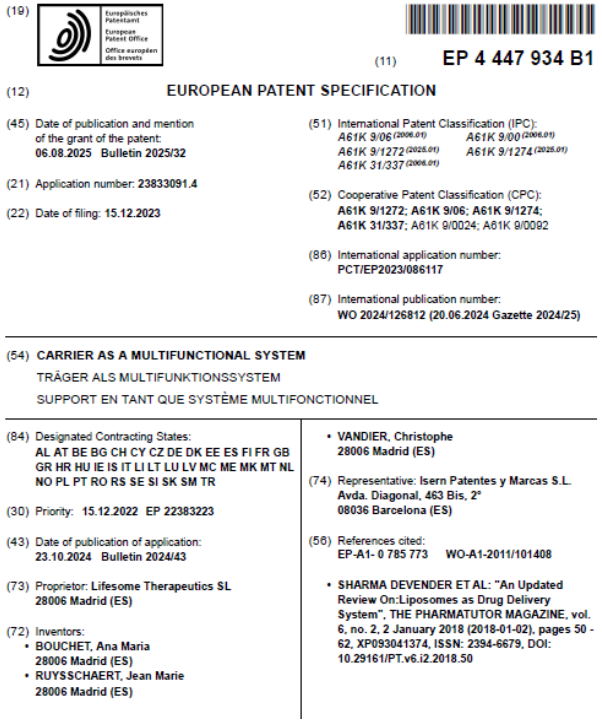

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(54) **CARRIER AS A MULTIFUNCTIONAL SYSTEM**
TRÄGER ALS MULTIFUNKTIONSSYSTEM
SUPPORT EN TANT QUE SYSTÈME MULTIFONCTIONNEL

(84) Designated Contracting States:
AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HR HU IE IS IT LI LT LU LV MC ME MK MT NL NO PL PT RO RS SE SI SK SM TR

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Hiermit wird bescheinigt, dass für die in der Patentschrift beschriebene Erfindung ein europäisches Patent für die in der Patentschrift bezeichneten Vertragsstaaten erteilt worden ist.

It is hereby certified that a European patent has been granted in respect of the invention described in the patent specification for the Contracting States designated in the specification.

Il est certifié par la présente qu'un brevet européen a été délivré pour l'invention décrite dans le fascicule de brevet, pour les États contractants désignés dans le fascicule.

Europäisches Patent Nr. · European patent No. · Brevet européen n°
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CARRIER AS A MULTIFUNCTIONAL SYSTEM

Patentinhaber | Proprietor(s) of the patent | Titulaire(s) du brevet

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Lopez de Hoyos 42
28006 Madrid
ES

PRIORITY: 2011

Freedom to **operate** on regards chemical synthesis and prevention of metastasis.

PRIORITY: 2023

Lifesome is the **sole owner** of the patent (EURO PCT granted on August 2025) **protecting** its **use** as antitumoral agent and nanocarrier for drug delivery of any therapeutical agent for any indication.

Lifesome THERAPEUTICS

3a - Pitfalls & Risks to consider:

Innovative mechanism (SK3 target) never demonstrated in humans.

Competing delivery platforms: alternative lipid or polymer systems may capture market preference due to established relationships.

Manufacturing and CMC complexity: lipid-based formulations can be technically demanding and expensive to scale to GMP.

Regulatory and safety risks: unexpected toxicology or biodistribution results can delay or halt programs.

3b – Opportunities & Mitigation plans:

Exclusive position in terms of development.

Ohmline is a **technology platform** in addition to a drug delivery system.

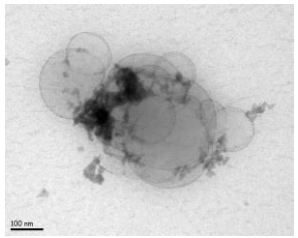
Ohmline's features do not add **increased complexity** to already established systems.

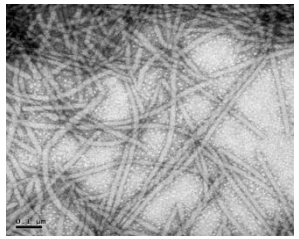
EMA's Innovation Task Force supported the clinical development of Ohmline-Docetaxel combination as a treatment for CRPC (meeting held on 16th December 2024).

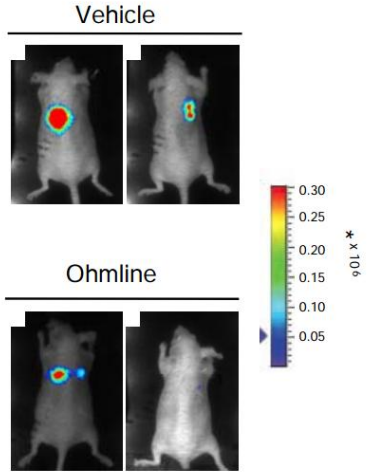
Lifesome THERAPEUTICS

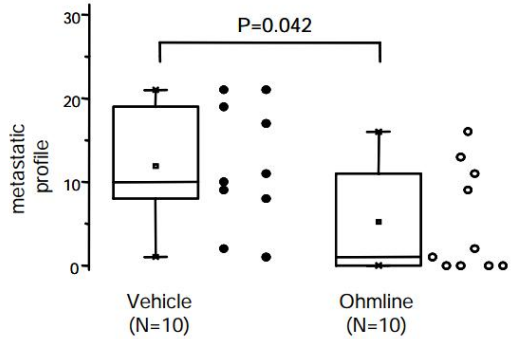
3 - PARTNERING OPPORTUNITIES: what does Lifesome offer?

- **Team expertise** in active lipids Biophysics and ion channel physiology.
- **Unique** drug delivery **tecnology** with synergistic anti-tumoral effect.
- **Patent protection.**
- **Enabling platform technology**: combination with toxicological high risk drugs in development.
- **Cost-effective manufacturing**.
- **Feasibility of market access**: competitive cost of combination with chemotherapy drugs.
- **Encapsulation capabilities** tailored to every specific cargo.









Lifesome THERAPEUTICS

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Your opportunity to shape tomorrow's medicine. Join us!!

Thank you!

Ana Bouchet

CEO

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