Programa Cooperación Farma-Biotech

Jornada IIb: **Oncología**

SOM-0777, a new chemical entity as αvβ3/αvβ5 integrin inhibitor for the treatment of glioblastoma

Madrid, 12 de mayo de 2011

CataloniaBIO
Associació catalana d'empreses de biotecnologia

MEDICAMENTOS INNOVADORES
Plataforma Tecnológica Española

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b) Innovative mechanisms of action
c) Differential features facing the market
d) Current status of development
e) IPR protection
f) Pitfalls & Risks to be considered

3. Availability for cooperation

The Company: Who is on board ?

The **Team**

Raúl Insa, CEO, Founder
- Medical doctor in Clinical Neurology
- MBA -ESADE, PDD – IESE, HARVARD
- 21 years: Parke-Davis, UCB, Uriach, ISDIN

Ignasi Belda, Founder
- PhD Informatics. University of Barcelona - BSP
- 10 years: IRB, Astra-Zeneca, U. Illinois
- Founder of Intelligent Pharma SL

Núria Gavaldà, Project Coordinator
- Doctor in Biology
- 6 years: U. de Cardiff

Núria Reig, Project Coordinator
- PhD in Biochemistry
- 7 years: USA and Suisse (Biotech)

Marc Centellas, Project Coordinator
- BS in Pharmacy
- 6 years; Ceva, Alcon-Cusi, Ferrer, Palau

Ramón Morera, CFO
- Venture capital firm Innova31

Strategic Board

Ernest Giralt, PhD
- Professor of Organic Chemistry
- University of Barcelona

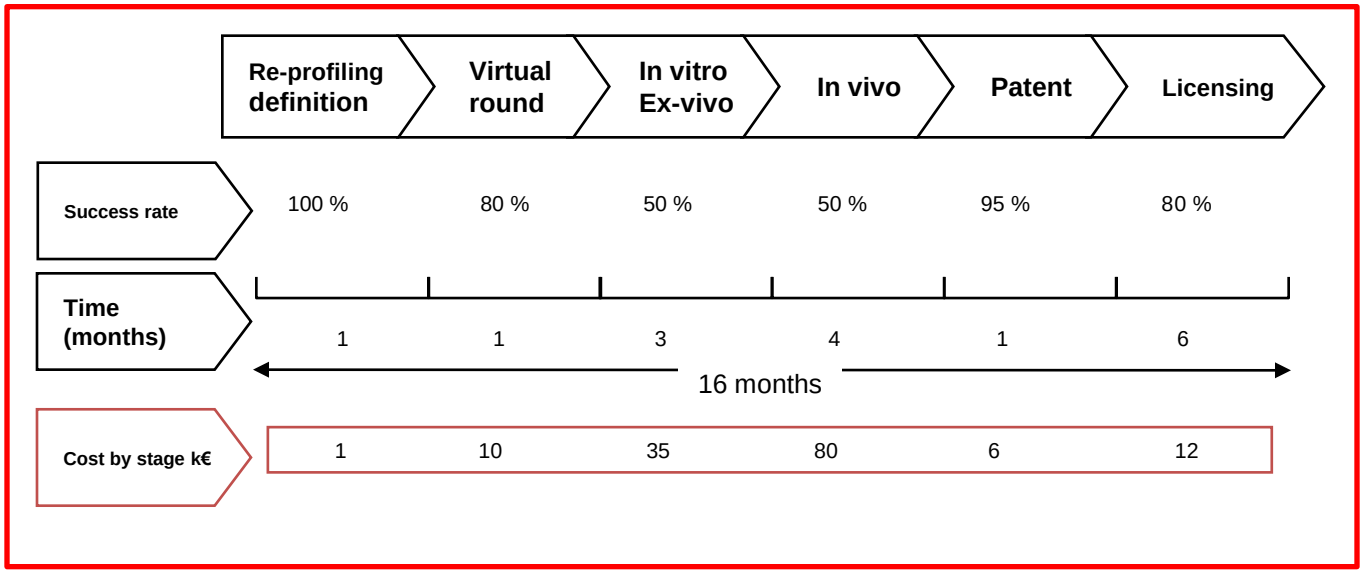
Joaquim Trias, PhD
- Bio entrepreneur (5 biotechs)
- San Francisco, CA

Hermann A.M. Mucke , PhD
- Ex R&D Vice-president at Roche
- University of Austria

David Alcraft, PhD
- Bridgehead International consultant
- Pharma sector specialist

Ad-hoc experts per project

The Company: Business Model



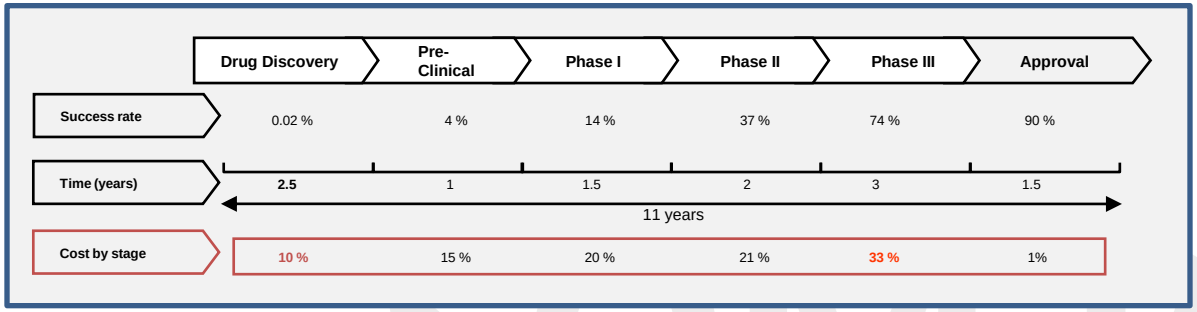
Time: 9-18 months

Cost/pj: 120 K €

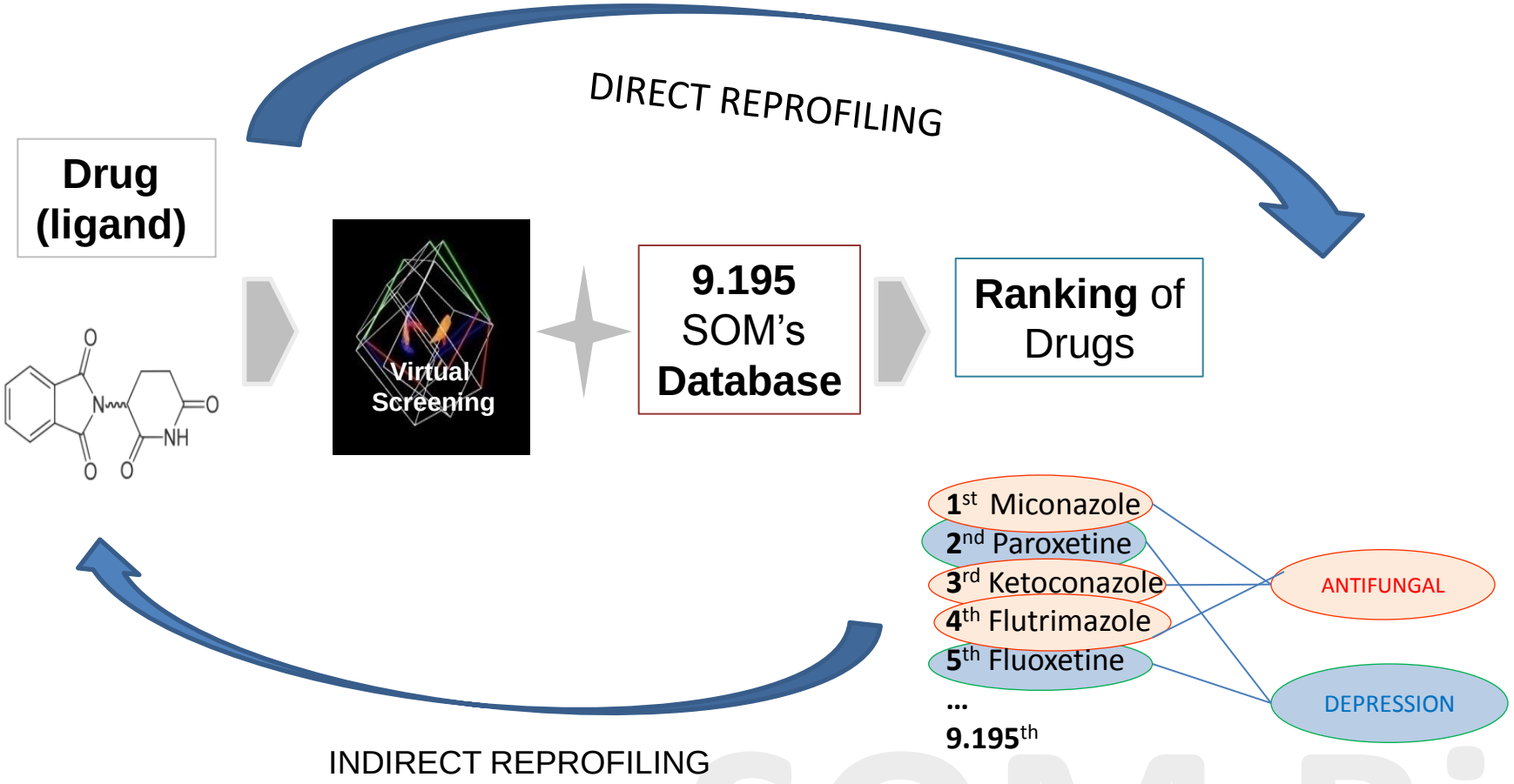
Price:

Up-front	400 K€
POC Phase II	800 K€
Registration	1.200 K€
Launch	1.600 K€
Royalties	5 %

Classic Pharma



The Company: Repurposing Technology



The Company: Pipeline

May 2011

Indication	Code	Discovery	In-Vitro	In-Vivo	Clinical	Patent	Comments
Asthma/COPD	SOM-1033					4Q'11	Inhaled formulation
Asthma/COPD	SOM-0525					US Filed	WW. Inhaled formulation
Dermatitis	SOM-0842					3Q'11	Topical application
Antibiotic	SOM-1025					EU Filed	Resistant strains
Oncology	SOM-0777					3Q'11	New scaffold. Glioblastoma
Anticoagulant	SOM-0720					3Q'11	Thrombosis prevention
AIDS	SOM-0856					2Q'11	Safer anti AIDS profile
Osteoporosis	SOM-0420					2Q'11	Oral formulation
M. Sclerosis	SOM-0999					4Q'11	Orphan drug
Malaria	SOM-0888					3Q'11	Resistant strains
Psoriasis	SOM-0666					3Q'11	Topical product
Phenylcetonuria	SOM-7400					4Q'11	Orphan disease
Amiloidosis	SOM-0226					4Q'11	Orphan disease
T-Cell Lymphoma	SOM-0666					4Q'11	Orphan disease

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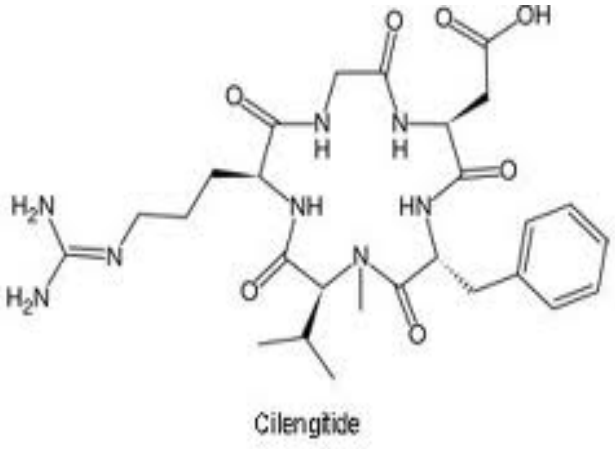
SOM-0777: Therapeutic Focus



Why a small molecule molecular targeted therapy (MTT) in cancer?

- 12 approved, 287 in clinical development, 32 in late-phase
- Of these αVβ3 - αVβ5 integrin (-) under dev. only 4. One launched
- Pfizer, Novartis, BMS & Merck are key players
- Small molecules MTT forecast sales is 3.635 m $ for 2019

Objective: Find new compounds with similar activity to Cilengitide (Merc KGaA), which is an αVβ3 - αVβ5 integrin and angiogenesis inhibitor in Phase III.

Indication: cancer, brain (Phase III, glioma)

cancer, non-small cell lung (Phase II)

cancer, squamous cell (Phase II)

cancer, head and neck (Phase II)

• Administration: 2.000mg i.v. twice /week. Many trials in combination with radio or chemo therapy.

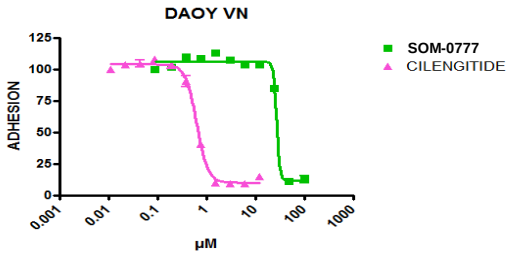
• Safety: Overall well tolerated (fatigue)

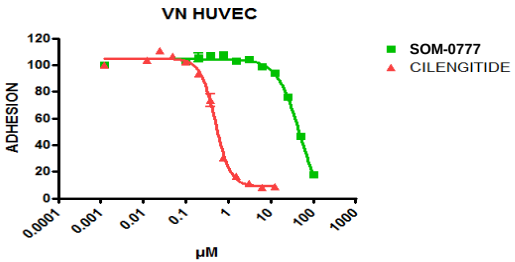
• **Indirect reprofiling on commercial & non-commercial drugs.**

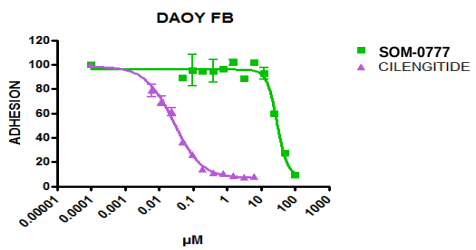
SOM-0777: Mechanism of Action

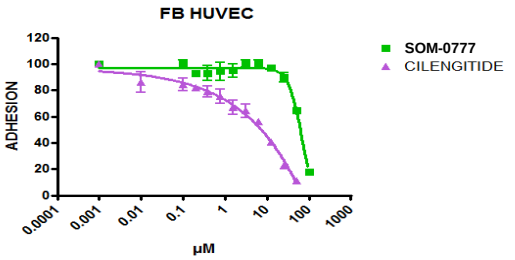
Inhibiton of cell adhesion was tested (1 hour) over HUVEC and Daoy cells in plates coated with vitronectin and fibrinogen. Control: Cilengitide. **SOM-0777 has αVβ3/αVβ5 integrin (-) activity.**

	Vitronectin		Fibrinogen	
	SOM-0777	**Cilengitide**	**SOM-0777**	**Cilengitide**
Daoy	27 µM (54 µM *)	0.6 µM (0.4 µM *)	30 µM	0.03 µM
HUVEC	50 µM	0.5 µM	29 µM	0.7 µM









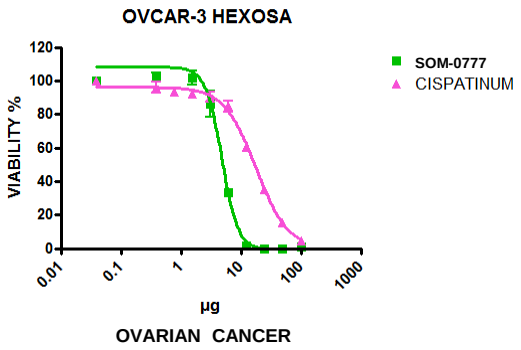
SOM-0777: Activity on Cellular Lines

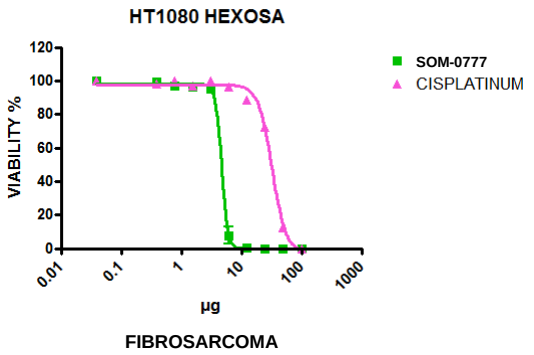
A viability assay was done by studying the effect at 72h over a panel of tumor cell lines: BxPC3 (pancreas), PC3 (prostate), OVCAR3 (ovary), HT1080 (fibrosarcoma), A549 (lung), MCF-7 (breast-Her2 positive), MDA-MB-468 (breast), SW480 (colorectal), and endothelial HUVECs. A serial dilution of compound SOM-0777 (starting at 100 µM, 1:1 dilutions) was evaluated. Two detection methods were used, Alamar (mitochondrial activity, that measures attached cells and in suspension) and hexosaminidase assay (only attached cells). Cisplatin was used as a positive control of the assay.

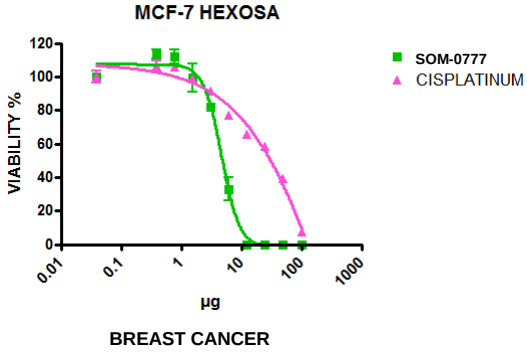
EC50 µM (% dead cells at 100 µM)	ALAMAR		HEXOSAMINIDASE	
	SOM-0777	Cisplatinum	SOM-0777	Cisplatinum
Daoy	9.4 (100)	nd	5.7 (100)	Nd
BxPC3	8.2 (100)	11 (100)	11 (100)	10 (99)
PC3	≈ 70 (67)	7.9 (100)	39 (59)	6.5 (100)
OVCAR-3	7.0 (100)	41 (77)	4.8 (99)	18 (95)
HT1080	4.7 (100)	16 (94)	4.7 (100)	32 (100)
MCF-7	6.1 (100)	≈ 50 (81)	4.7 (100)	≈ 50 (92)
MDA-MB-468	12 (100)	1.4 (100)	11 (99)	4.4 (99)
A549	6.0 (100)	5.9 (100)	4.6 (99)	4.4 (99)
SW480	5.9 (100)	28 (79)	5.6 (100)	27 (85)
HUVEC	15 (100)	25 (68)	6.8 (99)	≈ 100 (72)

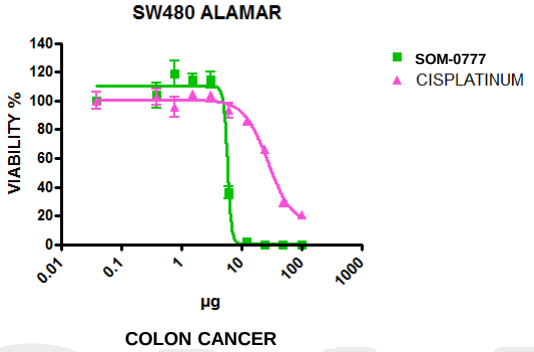
SOM-0777: Activity on Cellular Lines

SOM-0777 effect over cell viability with EC50 values from 4 to 11 μM, better than Cisplatinum in **ovarian**, **breast**, **colon** cancer and **fibrosarcoma**.



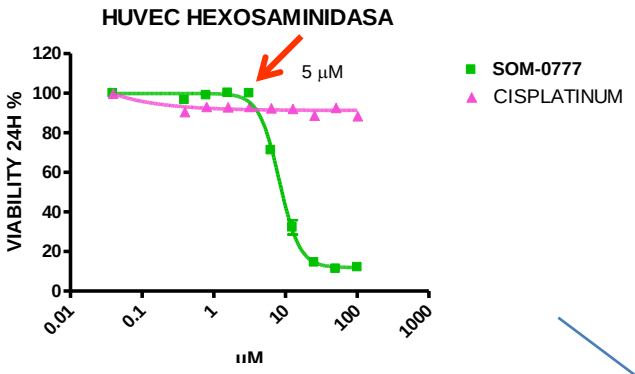




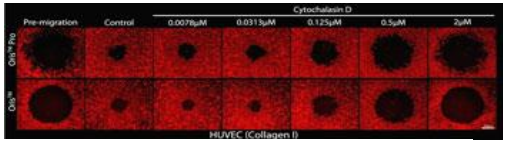


SOM-0777: Activity on Cell Migration

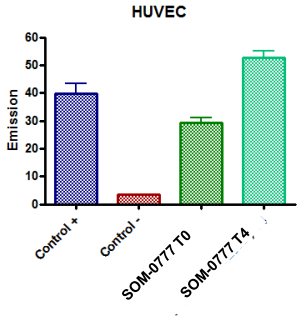
SOM-0777 **inhibits cell adhesion but not cell migration**.

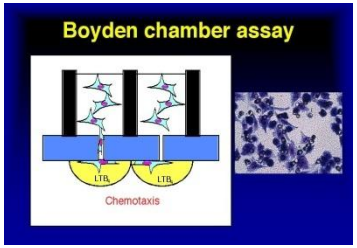


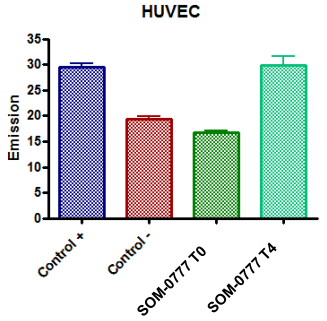
Maximum concentration for cell viability



ORIS migration assay

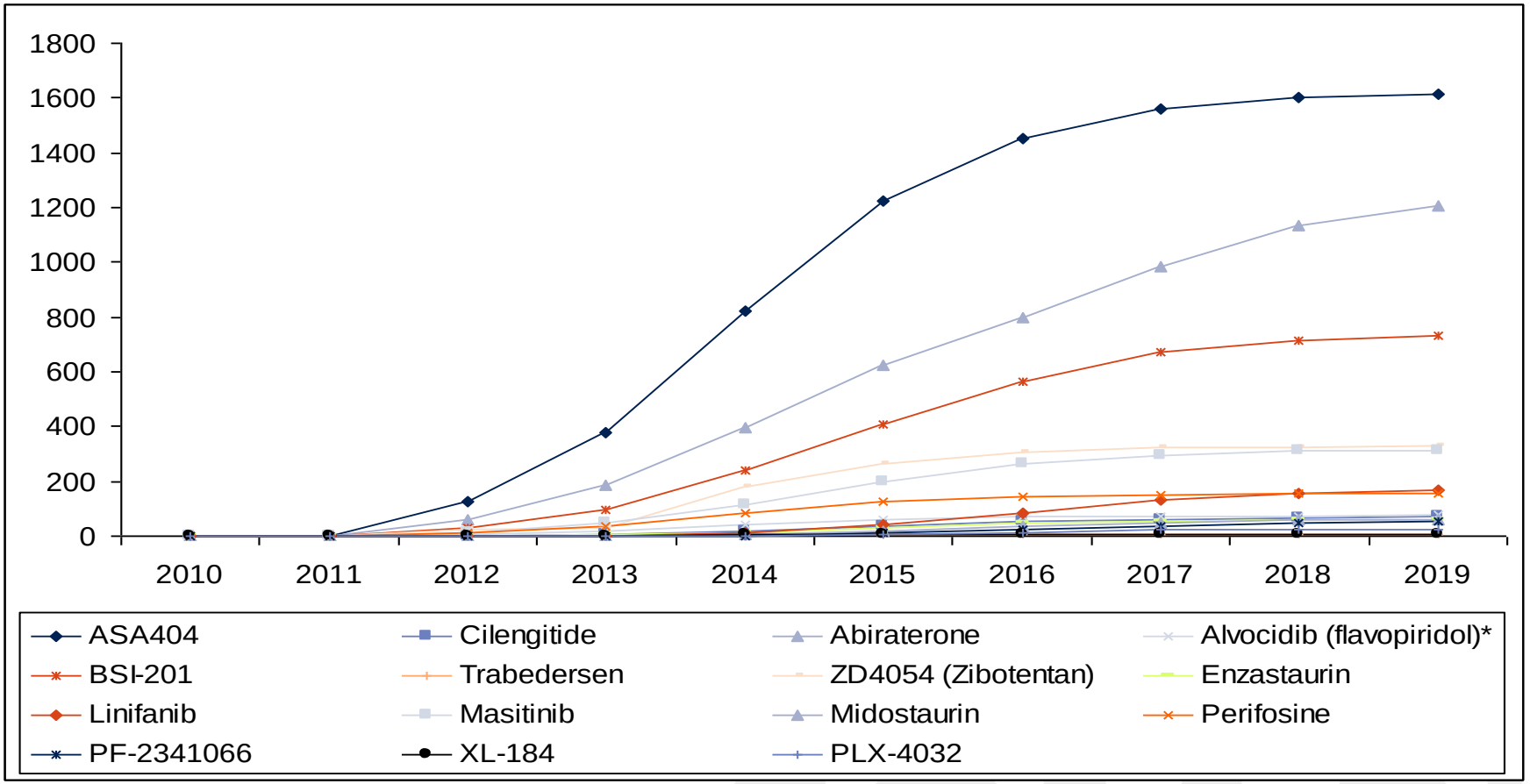






SOM-0777: Market Features

By 2019, small molecule MTTs in the late-phase pipeline will inject around **3.635 m $** into the cancer market.



Late-phase pipeline small molecule MTT sales ($m) for cancer in the seven major markets, 2010–2019

SOM-0777: IP, Pitfalls & Risks

SOM-0777 Characteristics:

- αVβ3/ αVβ5 integrin inhibitor that inhibits cell adhesion, not cell migration and is substantially better than cisplatinum in ovarian, breast, colon and fibrosarcoma cellular lines of cancer.
- It is not a commercial drug. Never administered to humans.
- New Chemical Entity. *Hit* compound for *lead* optimization; **Drug Discovery.**
- Mol. weight: 570.72 .
- LogP: 6.93.

Intellectual property:

A patent covering SOM-0777 and similar structural analogues is under writing. Patent will cover undisclosed chemical structures and medical use in cancer.

SOM-0777: Ready for licensing out

SOM's Business model is not to develop NME.

- SOM-0777, a NCE as αVβ3 integrin inhibitor active on ovarian, breast, colon and fibrosarcoma cancer is available for **licensing or sell out.**

- Chemical structure, in-vitro data, *know-how* and product sample is available under request and after CDA / MTA agreement.

- SOM Biotech is open to any collaboration on this specific product or any other oncology products under development (we have an orphan disease program on T-Cell Lymphoma).

Bioincubadora
PCB-Santander

SOM BIOTECH

Thanks for your attention !

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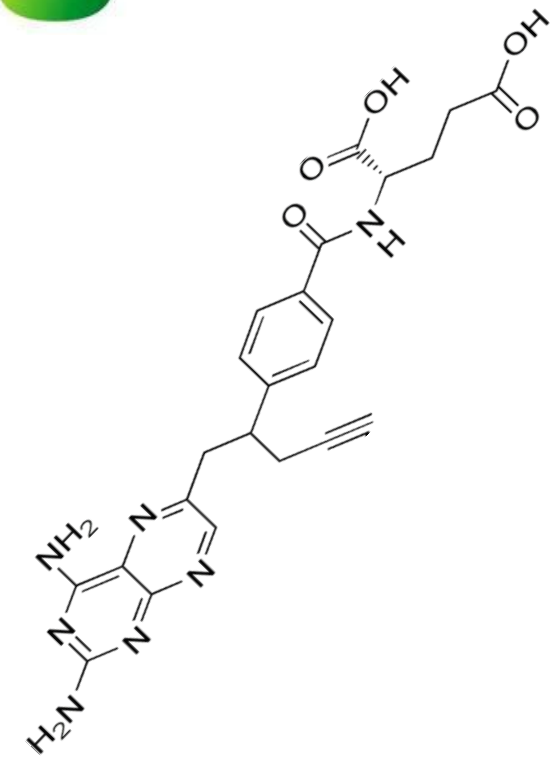
Peripheral T-cell T Lymphoma: vs Pralatrexate

ALLOS™ THERAPEUTICS



- MoA: a folate analogue metabolic inhibitor
- Indication: cancer, peripheral T-cell lymphoma (Launched, 2009-US)
  cancer, other indications (Phase II)
- Status: Orphan drug
- Administration: 190 mg i.v. 2x/week.
- Safety: Well tolerated

- **SOM-0666: Indirect reprofiling with drugs from SOM-CMC database.**

•In-silico results: available.

•Expected in-vitro results: September 2011.