LK-3: anti-S100P monoclonal antibodies for anti-cancer and anti-metastasis therapy

LYKERA biomed

Bilbao, 21 de septiembre de 2012

biospain 2012

Content

1. **The Company**
2. **The Product**
   a) Target Indications
   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. **Partnering Opportunities**

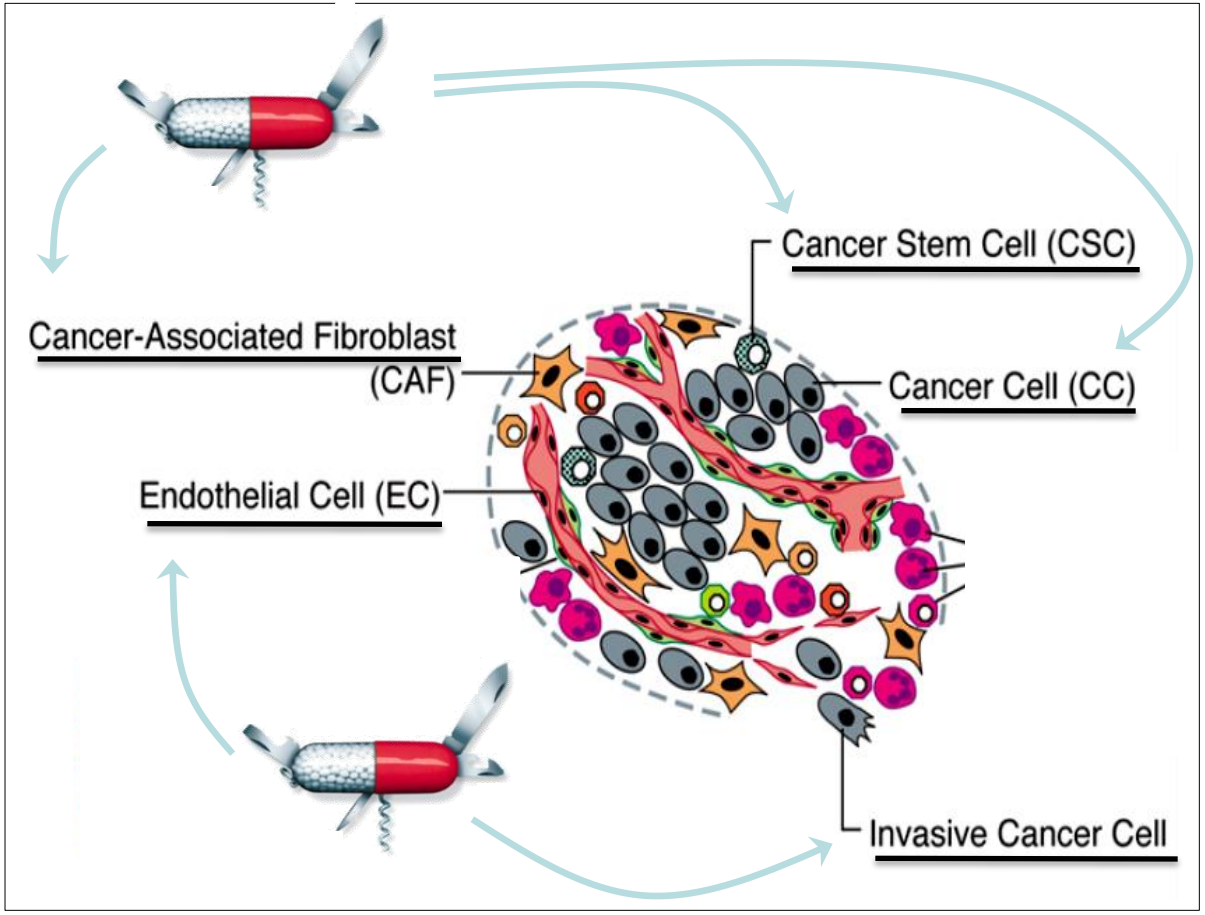
The Company

1. Lykera Biomed is a new company with headquarters in Barcelona. Lykera is a spin-off company by Leitat.
2. The company focuses its activities to the treatment and diagnosis of cancer.
3. Develops innovative drugs (especially biologicals) with triple activity, against:
    a) tumor cells,
    b) stromal compartment of the tumor, and
    c) tumor angiogenesis.

Target
&
Biomarker
identification

Where?
Tumor compartments:

Cancer Cell
Cancer Stem Cell
Stroma
Vascular
Metastasis



Adapted from
Hallmarks of cancer: the next generation. Hanahan D, Weinberg RA. Cell. 2011 4;144(5):646-74

- Our focus: **targeted drugs**, **targeting systems**, **molecular diagnosis** and **personalized medicine**.

- Wet work is performed at the **BIOMED DIVISION** of the **LEITAT TECHNOLOGICAL CENTER**.

LEITAT Technological Center
managing your technologies
member of TECNIO
Be tech. Be competitive

Biomed Division

- Once the invention is patent protected, it is transferred to **LYKERA BIOMED**.

Therapeutic Pipeline

Therapy	Target	Drug	Lead Identification	Lead Profiling	Lead Optimization	Regulatory preclinc	Indication	Partnered with	Non-exclusive license to
LK-1	S100A4	MAb			X		Solid tumors (pancreas, colon, melanoma & others)		
LK-2	VNR	RGD peptide		X			Tumor targeting		
LK-3: S100P MAb					**X**		**Solid tumors**		
LK-4		DNA technology		X			Solid tumors		
LK-5		MAb			X		Solid tumors		

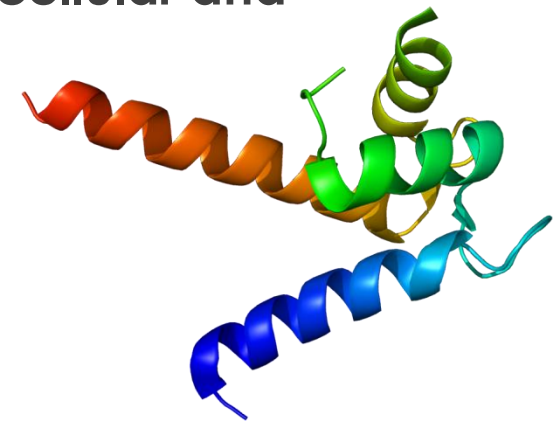
Diagnosis Pipeline

Diagnosis	Biomarker Validation	Assay development	Biomarker Clinical Proof of concept	Experimental Kit validation	Biomarker analysis	Clinical Kit validation	Indication
Biomarker	X	X	X	X	ELISA, WB, IHC		Multiple cancer types

The Target

1. **Target Nature**

   S100P is a 95 aa member of the S100 family of small calcium-binding proteins that have been reported to have intracellular and extracellular functions.



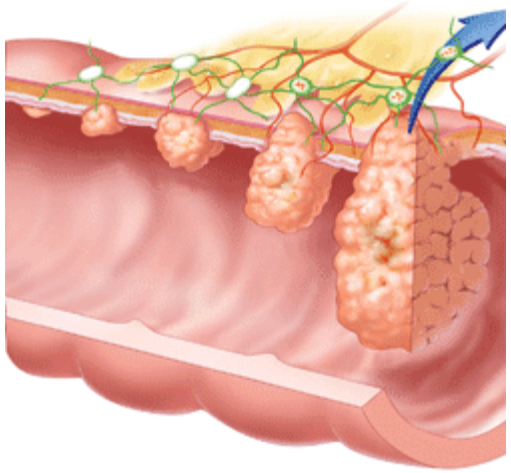
2. **Target Biology**

   Extracellularly interacts with RAGE

   At intracellular level binds to Ezrin

The Target

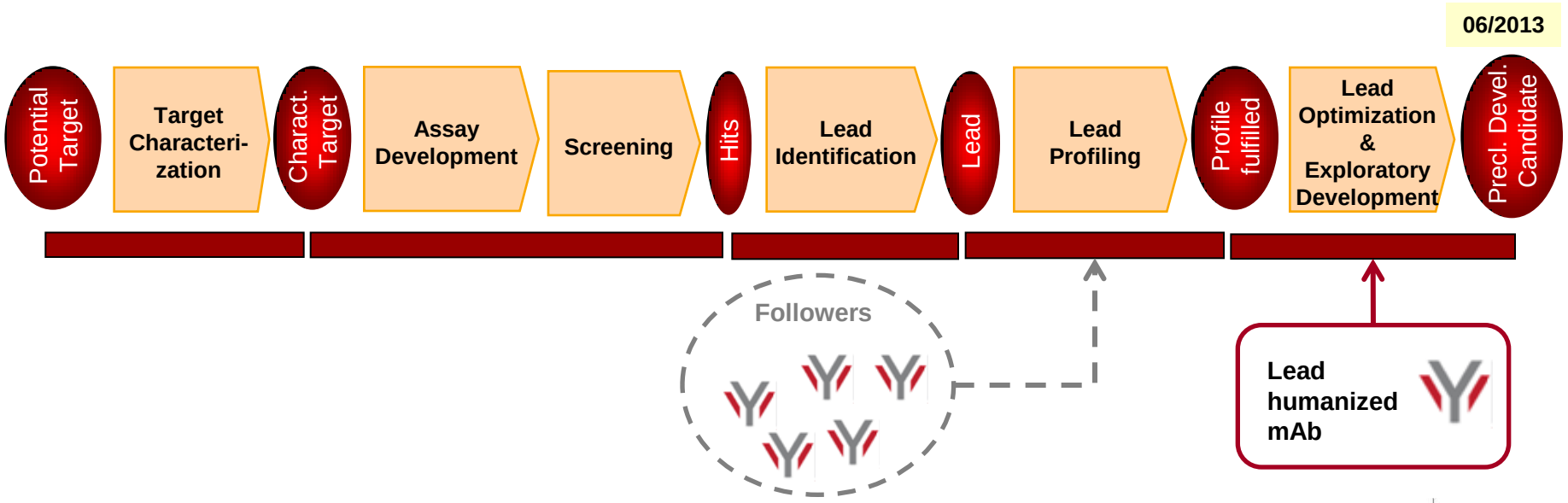
3. S100P is over expressed in several ***Target Indications:***
    a) Pancreatic, gastric, colorectal, ovarian, breast, lung and prostate tumors



4. Over expression promotes:
    a) Cell motility & invasion
    b) Cancer growth, survival & Tumor metastasis
    c) Tumor resistance to Chemotherapeutics
    d) Correlates with poor clinical outcomes

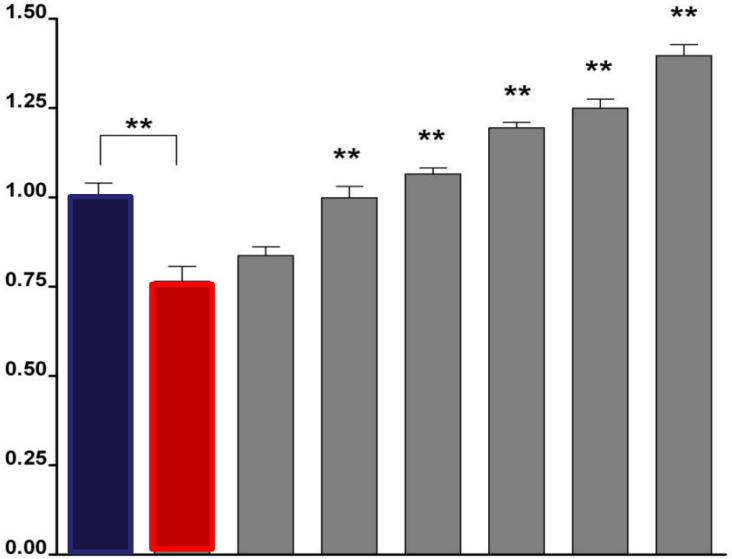
The Product

1. Anti-S100P monoclonal antibodies
   a) Generated in mice via hybridoma technology.
   b) Currently under humanization phases.

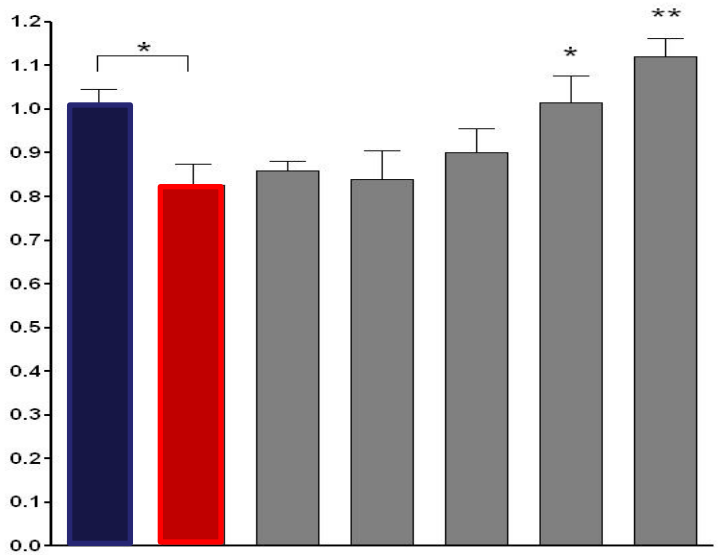


The Product (Innovative mechanisms of action)

1. S100P induces ***survival*** in the HT1080 human fibrosarcoma & in the BxPC3 human pancreatic cancer cells exposed to doxorubicin & gemcitabine respectively



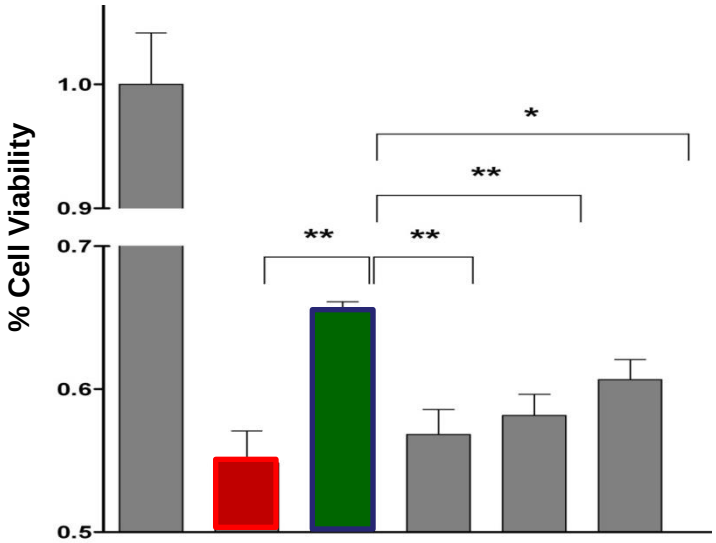
Doxorubicin (nM): -- 240 240 240 240 240 240 240
S100P (nM): -- -- 15 31 62 125 250 500



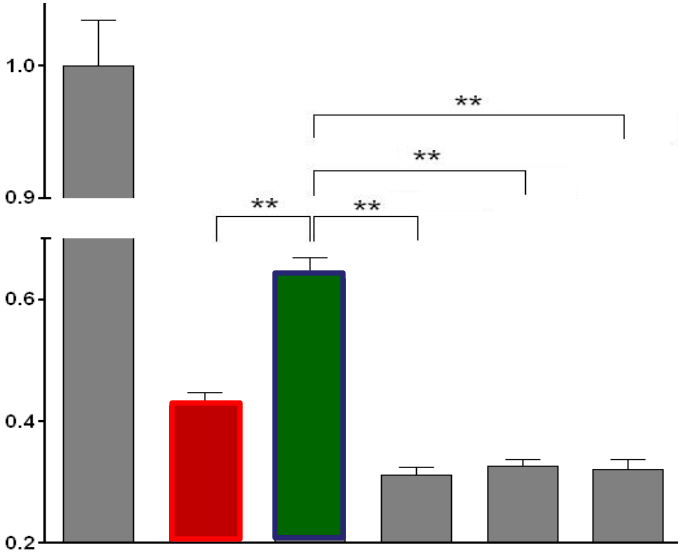
Gemcitabine (nM): -- 23 23 23 23 23 23
S100P (nM): -- -- 23 47 94 187 750

The Product (Innovative mechanisms of action)

2. Anti-S100P antibodies ***block*** S100P induced resistance to doxorubicin & gemcitabine in fibrosarcoma & pancreatic cancer



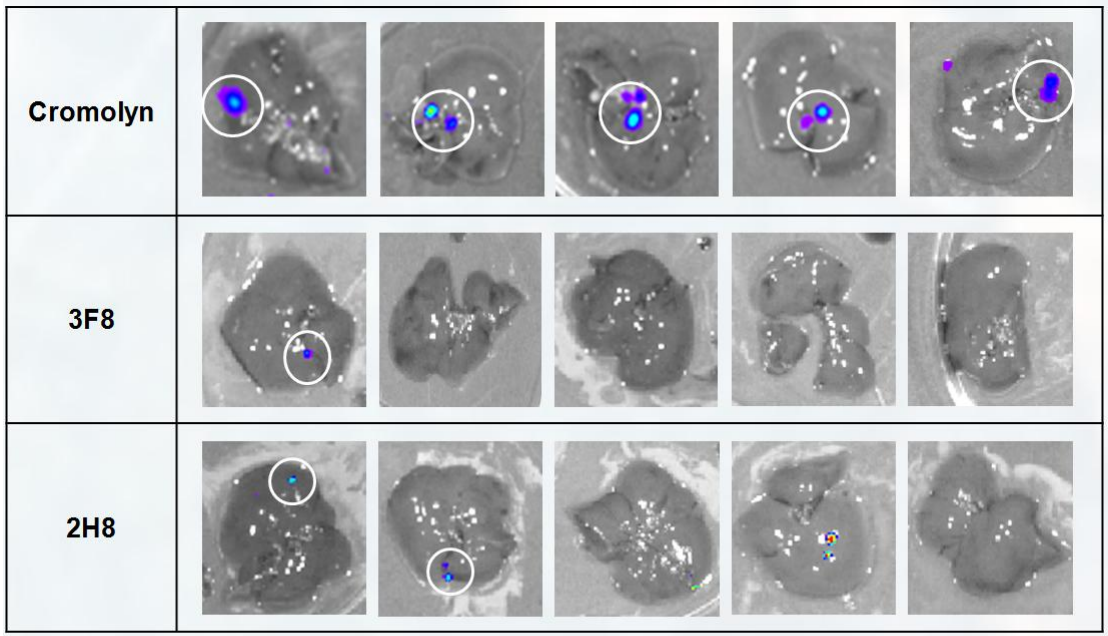
Doxorubicin (nM):	--	240	240	240	240	240
S100P (nM):	--	--	100	100	100	100
mAb 3F8 (nM):	--	--	--	500	--	--
mAb 1A5 (nM):	--	--	--	--	500	--
mAb 2H8 (nM):	--	--	--	--	--	500



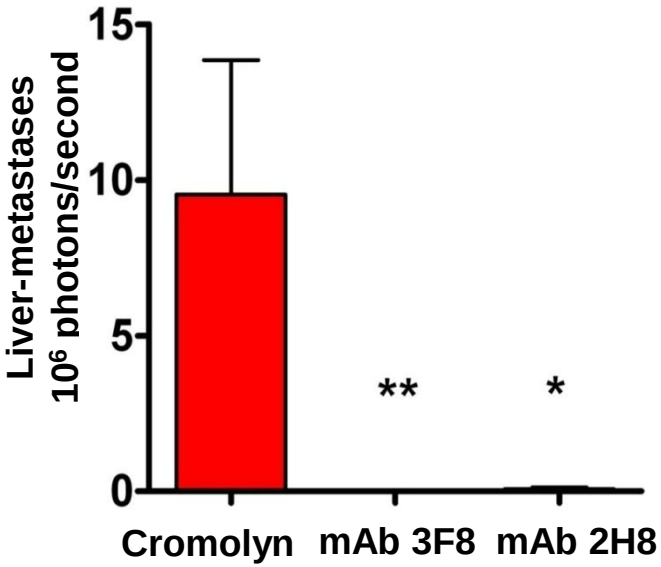
Gemcitabine (nM):	--	100	100	100	100	100
S100P (nM):	--	--	500	500	500	500
mAb 1A5 (μM):	--	--	--	1.2	--	--
mAb 2H8 (μM):	--	--	--	--	1.2	--
mAb 3E3 (μM):	--	--	--	--	--	1.2

The Product (Innovative mechanisms of action)

3. Anti-S100P mAbs ***block tumor growth and metastatic spread in*** *in vivo* orthotopic pancreatic model (BxPC3).



In vivo imaging of liver metastasis from animals treated with Cromolyn (reference compound) and mAb 3F8 and 2H8.



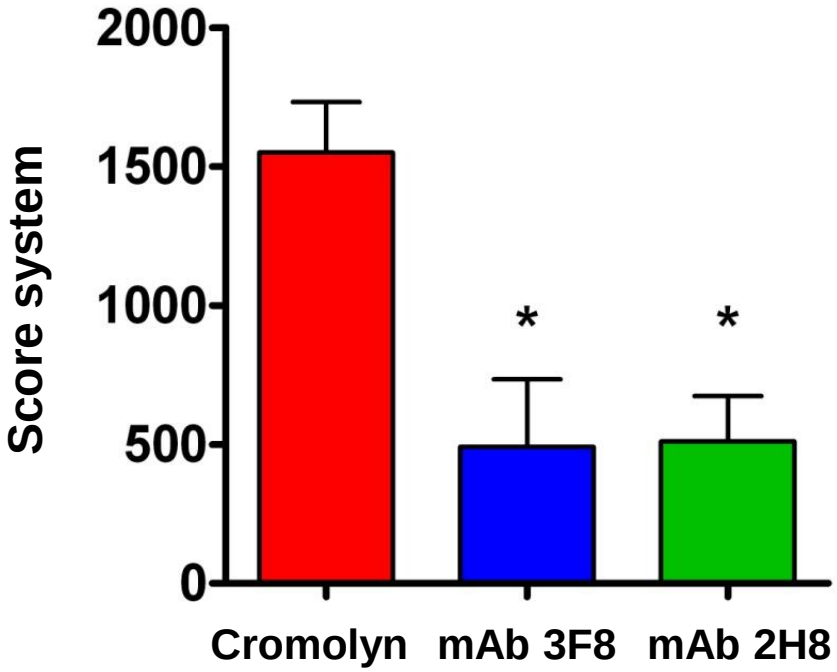
The Product (Innovative mechanisms of action)

3. Anti-S100P mAbs *block tumor growth and metastatic spread in vivo*.

Staging and Scoring System

Stage	Description	Score
Primary Tumor		
T_0	No tumor	1
T_1	Small tumor (tumor *d<7 mm*)	2
T_2	Large tumor without infiltration (tumor *d>7 mm*)	3
T_3	Large tumor with infiltration but still visible margins	4
T_4	Diffuse and infiltrating tumor	5
Organ Metastases		
M_0	No liver or lung metastases	1
M_{1Li}	Liver metastases	5
M_{1Lu}	Lung metastases	5
M_1	Liver and lung metastases	10
Peritoneal Metastases		
P_0	No peritoneal metastases	1
P_1	Less than five peritoneal metastases or one with *d<7 mm*	3
P_2	More than five peritoneal metastases or one with *d>7 mm*	4
P_3	Malignant ascistes	5
P_4	Diaphragm / kidney / intestine / adrenal metastases	$3+3+3+3+P_{0/1/2/3}$
Lymph Node Metastases		
N_0	No lymph node metastases	1
N_1	Peripancreatic lymph node metastases	3
N_2	Regional lymph node metastases (e.g., mesenteric, mediastinal)	5

Scores for the primary tumor (T), organ metastases (M), peritoneal metastases (P), and lymph node metastases (N) were multiplied to calculate the total tumor score for each animal. Score P_4 value is the sum of the corresponding P_0, P_1, P_2, P_3 ($P_{0/1/2/3}$) plus an additional value of 3 for metastasis presence in the diaphragm, 3 for kidney, 3 for intestine and 3 for adrenal glands



TMPN classification and scoring system. Based on *Hennig R. et al. Neoplasia 2005. 7(4): 417-25* with modifications.

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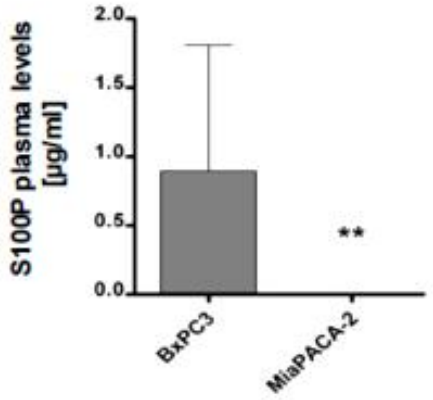
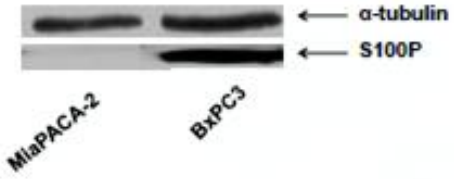
The Product (Innovative mechanisms of action)

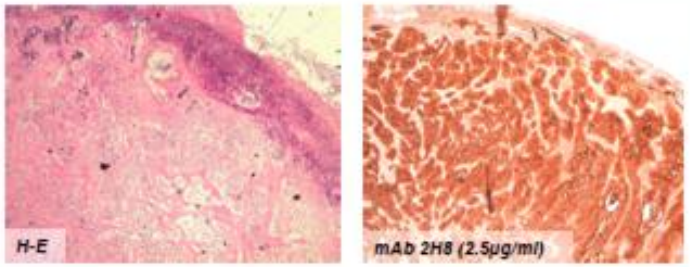
4. Anti-S100P mAbs allow for S100P quantification in plasma samples and have additional features for diagnostic purposes (ELISA, WB, IHC)



ELISA quantification of S100P plasma levels in mice bearing tumors of the indicated tumor cell lines. Graph shows mean ± s.d. *Mann whitney U-test* ** $p<0.01$.



Western Blot analysis of S100P expression in two different human tumor cell lines. BxPC3 (positive expression) and MiaPACA-2 (negative expression).



IHC staining of S100P protein expression in subcutaneous tumor from BxPC3 cell line.

Differential features facing the market

1. **Triple mechanism of action of the anti-S100P mAbs:**
   - ✓ **Control tumor proliferation**
   - ✓ **Control the metastatic spread**
   - ✓ **Block the resistance to chemotherapeutic agents.**

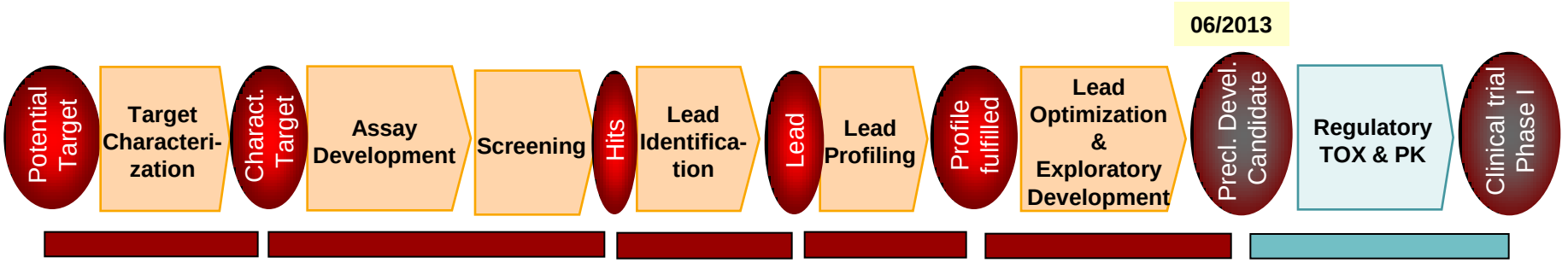
2. **Lykera's antibodies are "first-in-class"; there are currently no competitors developing antibodies to S100P**

IPR protection

1. **Patent protected:**
   - ✓ **"S100P ANTIBODIES FOR CANCER TREATMENT AND DIAGNOSIS"**
   - ✓ **Priority date: January 2012**
   - ✓ **PCT/ EP2012/050653**
   - ✓ **WO2012/098124**

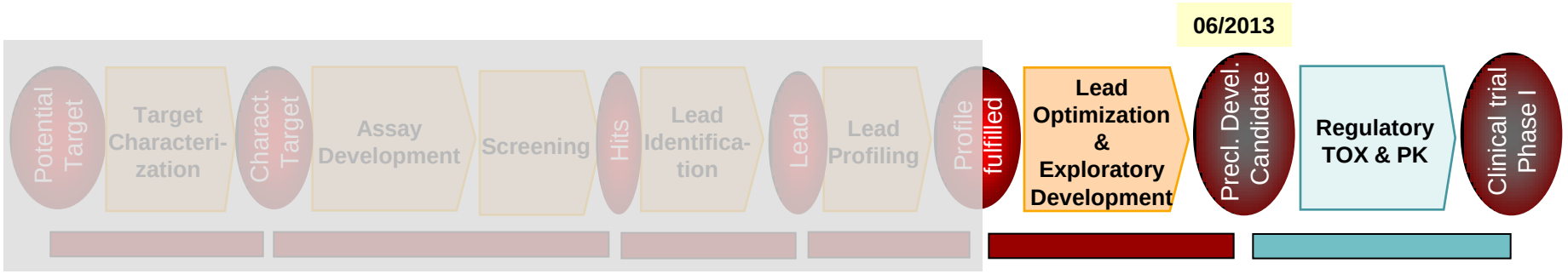
2. **Lykera Biomed is the sole owner**

Current situation



- ✓ S100P target is well validated *in vitro* & *in vivo*
- ✓ mAbs generated & characterized *in vitro* & *in vivo*
- ✓ Proof of Principle reached
- ✓ Full patent protection: general use of anti-S100P mAbs for therapy & diagnosis
- ✓ Clinical & market attractiveness proved (literature & own data)

Future steps



- ✓ Clone chimeric & humanized mAbs into a suitable CHO cell expression system: 6 months
- ✓ Produce & purify GMP: 6 months
- ✓ Regulatory preclinical TOX & PK: 1 year
- ✓ IND & Clinical trials

Pitfalls & Risks to be considered

1. Potential competitors:
   a) Cromolyn → less effective, no clear MoA
   b) siRNA → not ready yet
   c) RAP (Rage antagonist peptides) → PK issues

2. Preclinical Proof of Principle = Clinical Proof of Concept?

Partnering Opportunities

We are globally looking forward new *collaborations* for research partnerships, co-development, licensing-out, or joint-venture of our most advanced products in order to achieve our ambitious goals.

- License.
- Partial funding with a first refusal right option.
- Partnership for further progress towards the upcoming phases.
- Scientific collaboration.

Responsible Team

- José Luís Hernández
- Sheila Dakhel
- Laura Padilla
- Jaume Adan
- Toni Coll
- Manolo Rivas
- Josep Mª Martínez
- Laura Barberà
- Marc Masa
- Ramon Messeguer
- Carme Calvís
- Rosa Hervás
- Lourdes Roque
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LYKERA biomed

"Innovation for future health"

Thank you for your attention

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