STELLAR MEDICINES FOR RARE DISEASES

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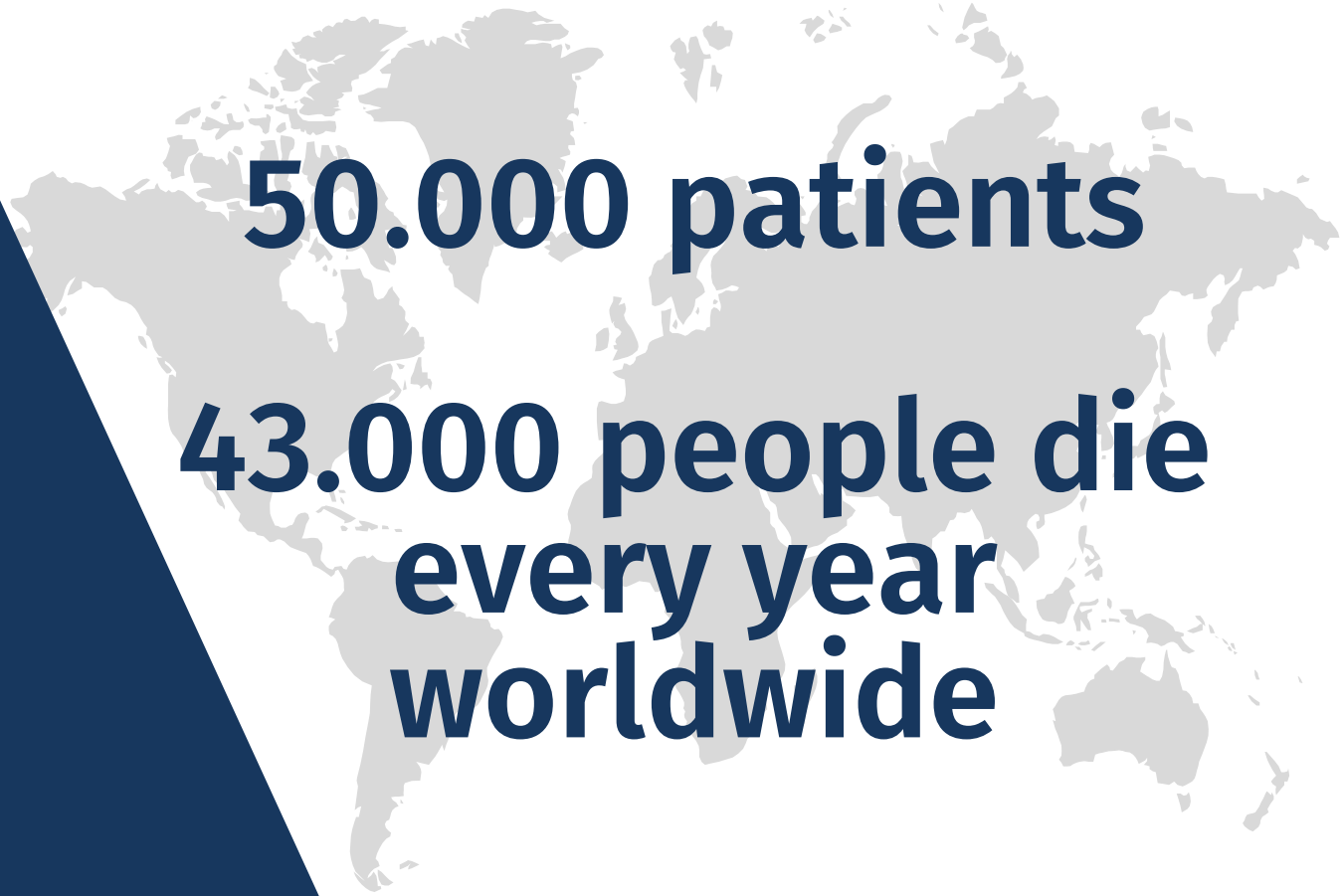
An effective targeted cancer therapy

PROBLEM

Malignant Pleural Mesothelioma (MPM) is a very aggressive pleura and peritoneum cancer and there is very high risk of local recurrence after surgery.

Patient have 12 months survival after diagnosis.



50.000 patients

43.000 people die every year worldwide

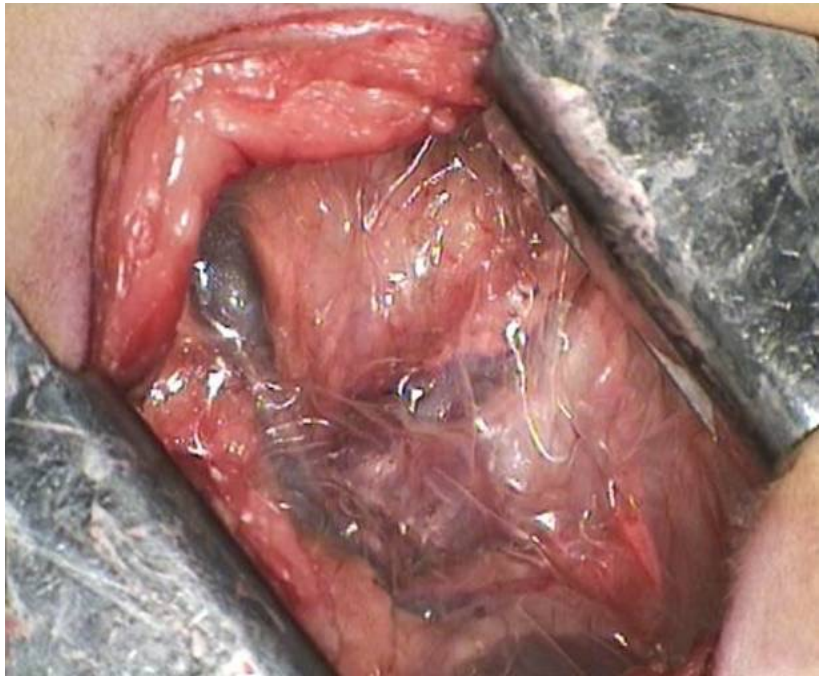
THE BIG IDEA

Development of novel medicine repurposing in innovative targeted delivery system s drugs used to cure Malignant Pleural Mesothelioma

Solution: HYALCIS

Hyalcis is a biodegradable film loaded with **cisplatin** and sodium hyaluronate.

The film is deposited in the thorax cavity after surgery for primary tumor resection, with the objectiv e to release **cisplatin in loco** to prevent or delay the local metastases of MPM.



Thickness :60-120 µm

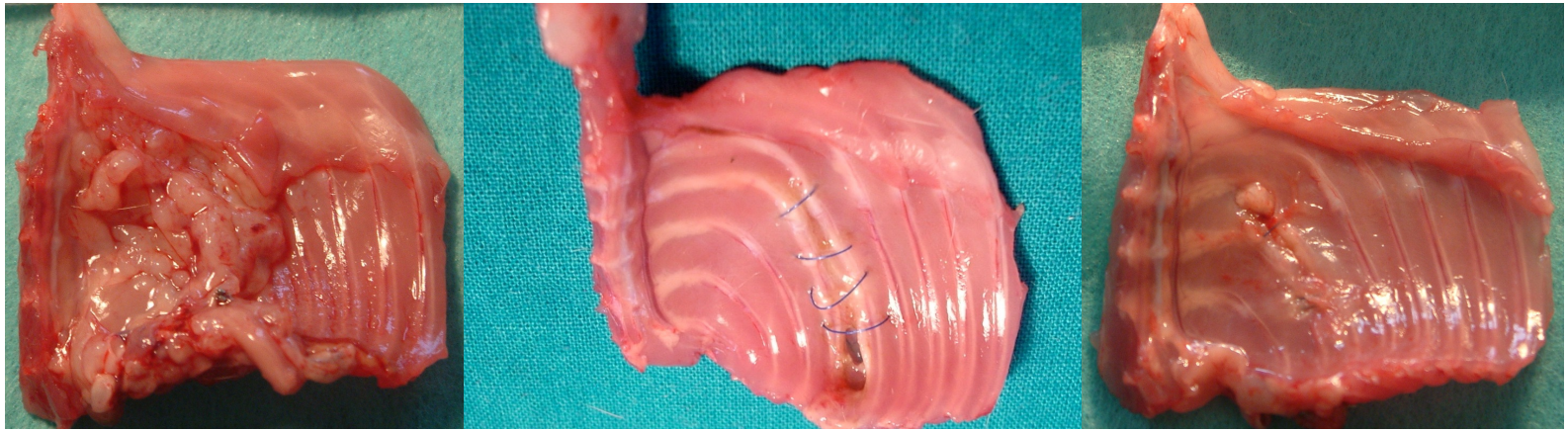
Size: 10x10 cm

Ampollini L. et al. Polymeric films loaded with cisplatin for malignant pleural mesothelioma: a pharmacokinetic study in an ovine model. J Thorac Dis 2017, doi: 10.21037/jtd.2017.10.74.

HYALCIS BENEFITS

Unique targeted *in situ* treatment

Untreated **Hyalcis film treatment** **Cisplatin solution**



Efficacy: **Significant reduction** of local tumor metastases
Liver and renal **toxicity lower** than IV administration

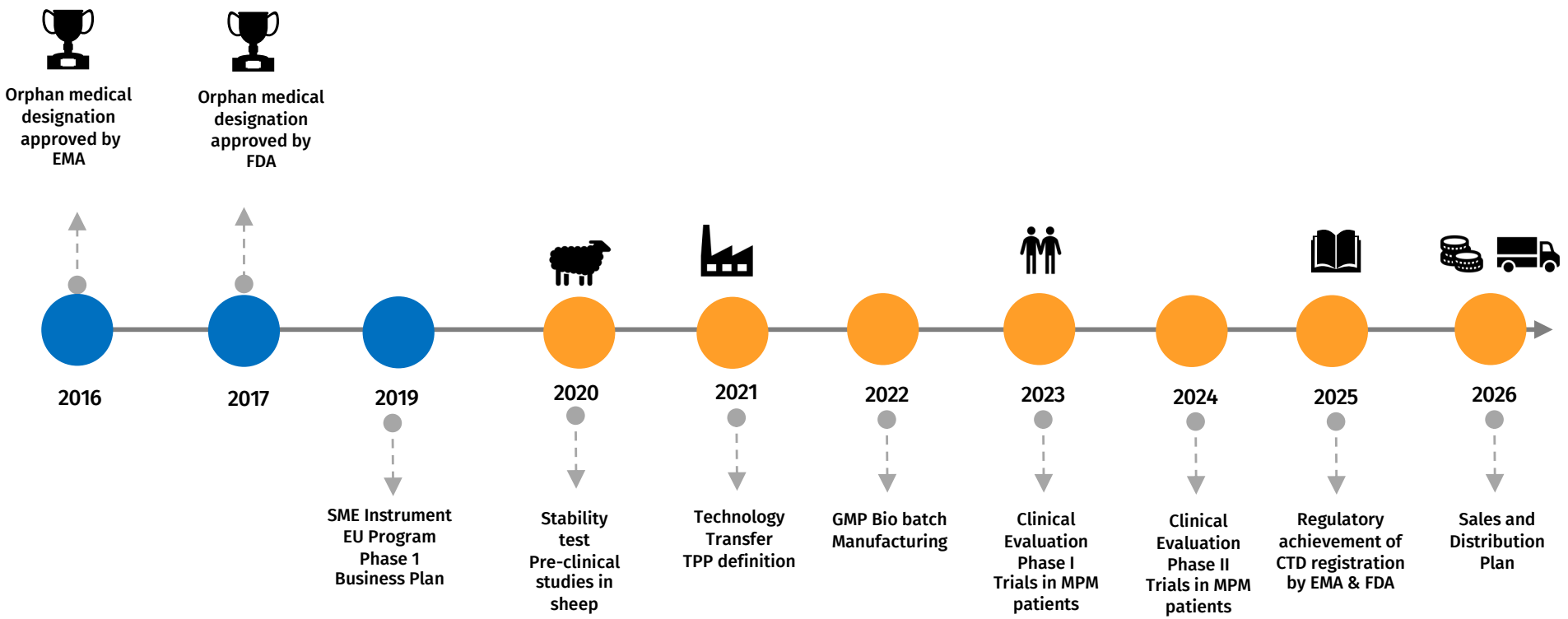
EXISTING ALTERNATIVES

Currently on the market there are **no product for in situ treatment** of malignant mesothelioma.

Alternative solutions include:

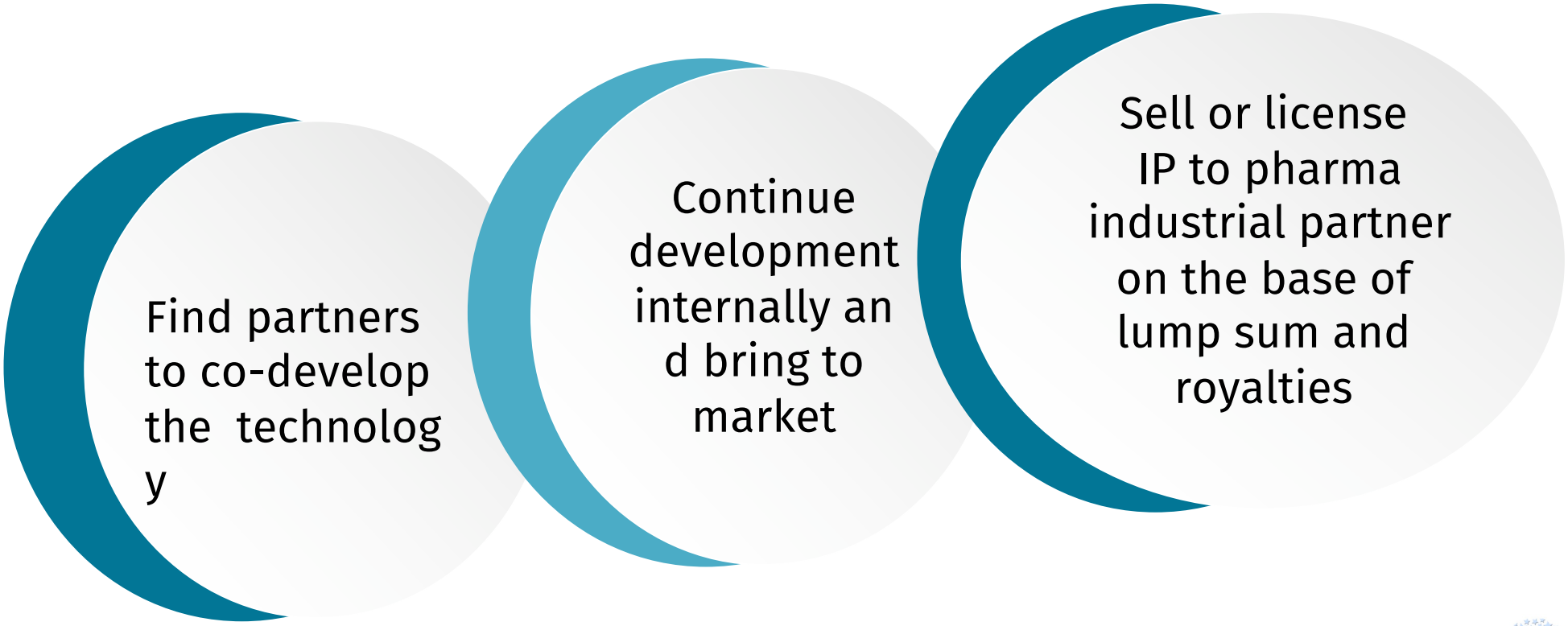
1. Radiotherapy, which remains a palliative method.
2. Intravenous cisplatin chemotherapy with some efficacy but strong adverse effects due to toxicity.
3. Intracavitary chemotherapy, still under test but with similar results as IV.

DEVELOPMENT PLAN

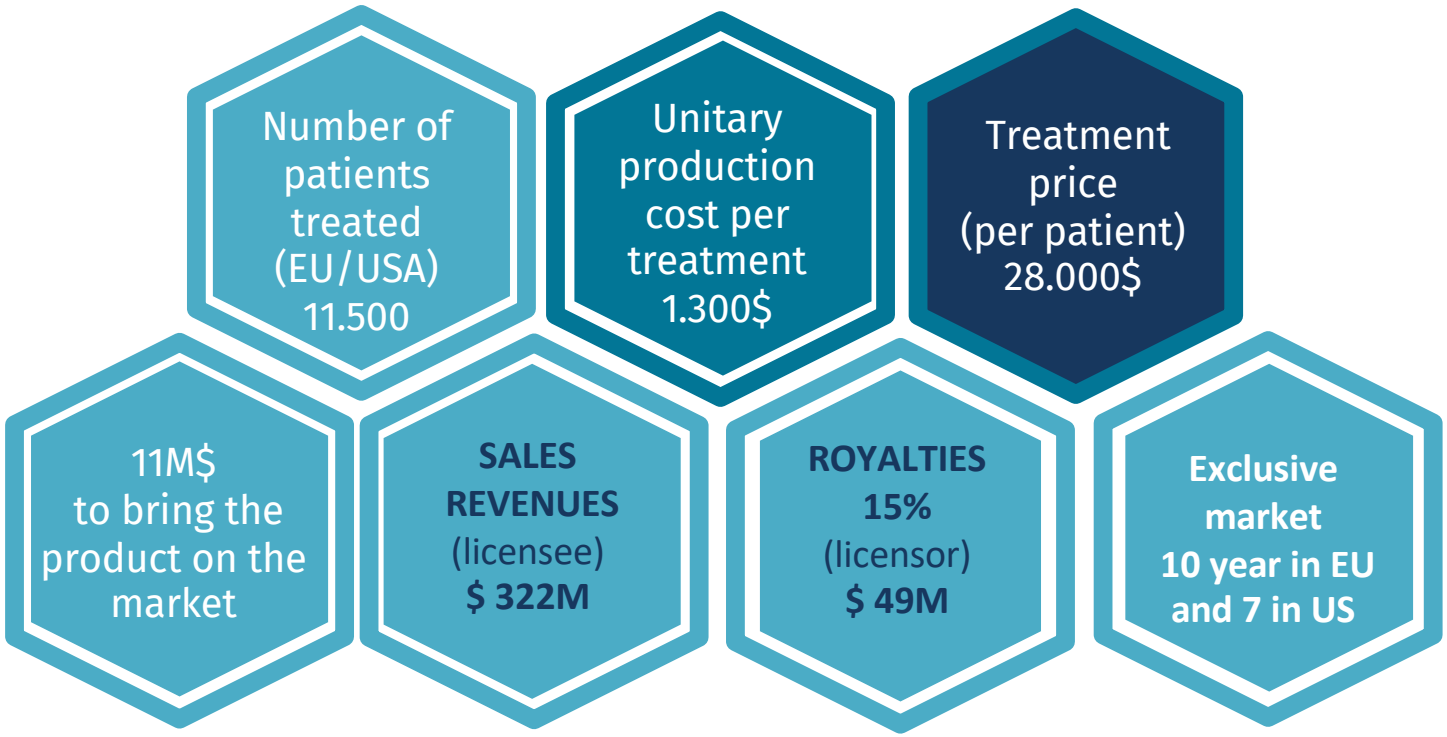


EARLY ADOPTERS AND CUSTOMERS

BUSINESS MODEL:CHANNELS



FINANCIAL OVERVIEW



DESCRIPTION OF THE PRODUCT

Hyalcis is a cisplatin loaded polysaccharide thin film, used as intrapleural implant for the local drug delivery on pleural surface during surgery

Cisplatin content: 0.5 – 1 % w/w
50 – 100 µg/cm^2

Thickness :60 - 120 µm

Weight: 8 - 12 mg/cm^2

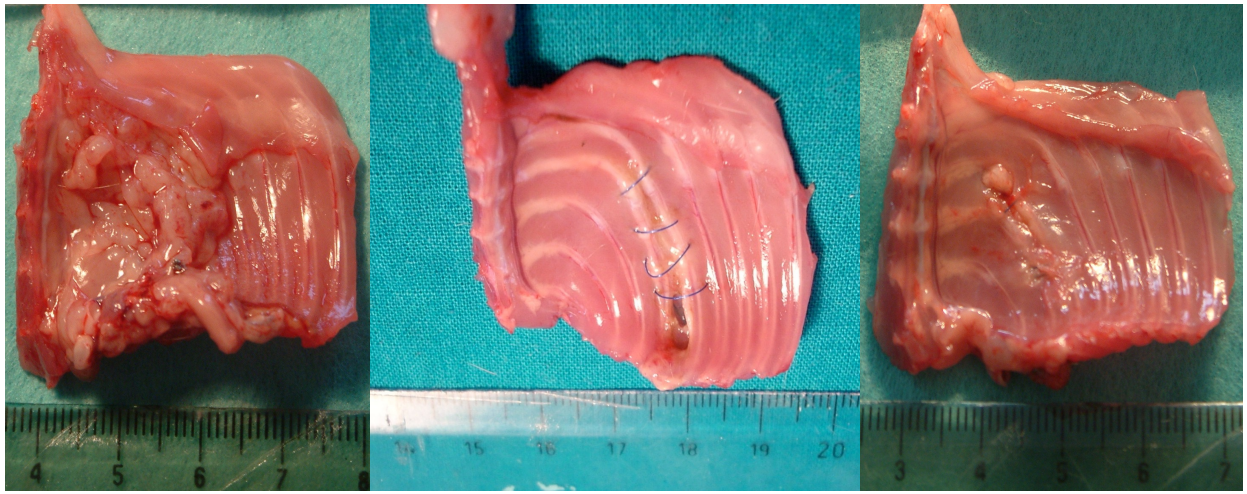
MEDICAL PLAUSIBILITY

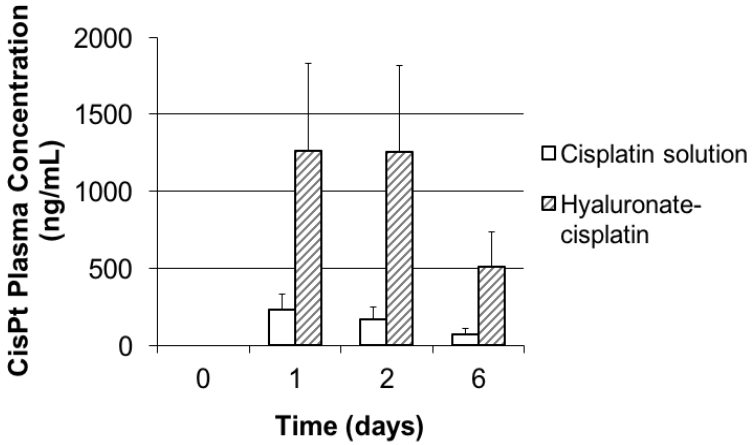
Hyalcis is for direct application on the mesothelium surface where it releases locally cisplatin

- High cisplatin local concentrations
- Prolonged exposure to the anticancer drug
- Improved efficacy for the local control of the disease
- Reduced systemic toxicity

MESOTHELIOMA RECURRENCE ON CHEST WALL

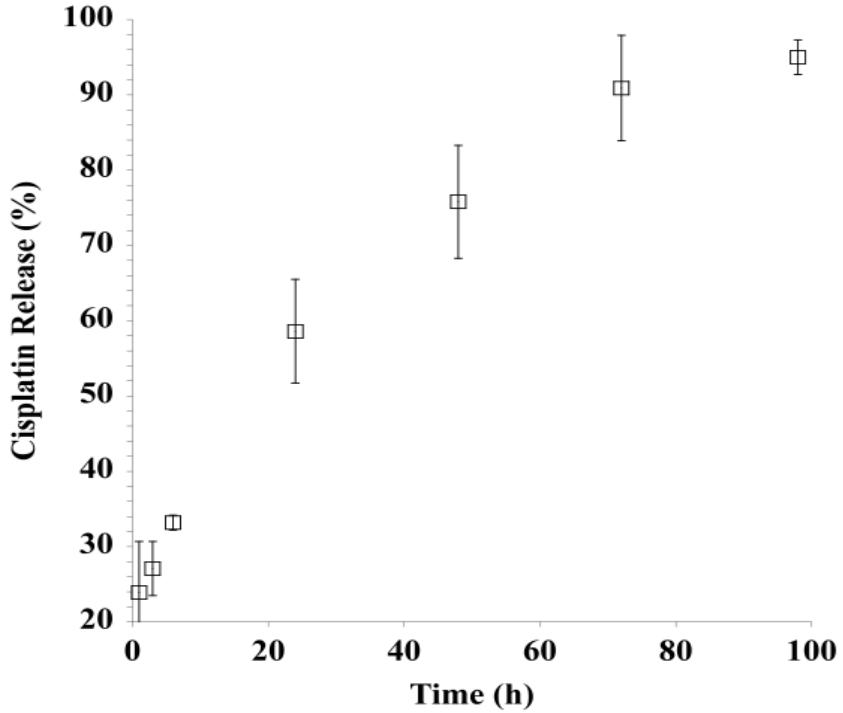
Untreated | CisPt HA film | CisPt IP solution





CISPLATIN RELEASE FROM HYALCIS FILMS

In vitro release conditions: Temperature = 37°C; 15 ml Saline Solution, Bath Shaker

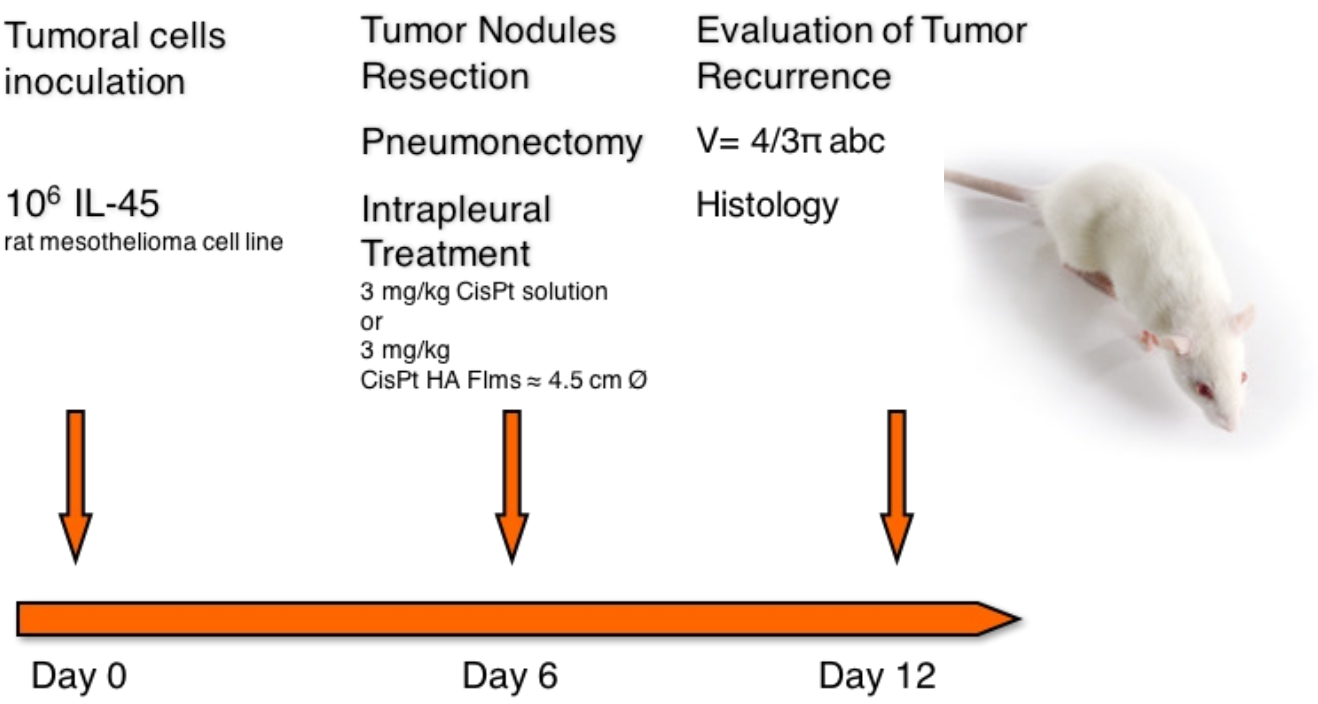


Controlled release of cisplatin over time as a result of the interaction with the pol ymer hydrated matrix formed.

In these conditions, the release is nea rly complete after 96 hours.

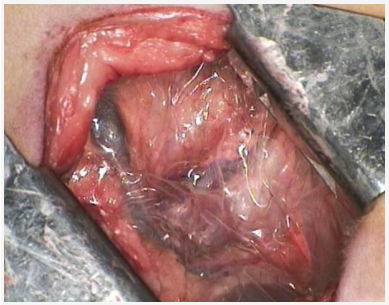
In vivo efficacy study in rats

A well-established orthotopic rat recurrence model of malignant pleural mesothelioma was used.



The PlumeStars product

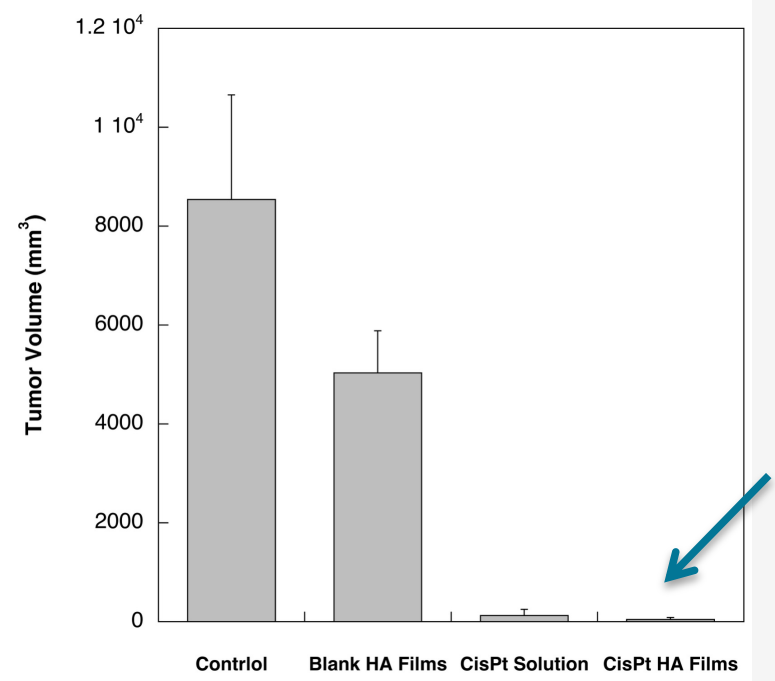
STELLAR MEDICINE FOR LUNG DISEASES



The product developed is a hydro philic, thin and flexible film, conta ining cisplatin drug.

The film is applied intrapleural du ring surgery, adhering to the mes othelial or epithelial surfaces.

The release of anticancer cisplatin from the film is prolonged, provid ing high local concentrations pre cisely in the site where the residu al tumor could develop.



Hyalcis efficacy study results

In vivo toxicity and PKs study in sh eep

- Sardinian sheep (40 Kg)
- Surgical treatment
  - *Left pneumonectomy*
- Adjuvant treatment (Cisplatin 3 mg/kg)
  - *Intrapleural Hyalcis films*
  - *Intrapleural cisplatin solution (IP)*
  - *Intravenous ciplatin solution (IV)*
  - *Control*

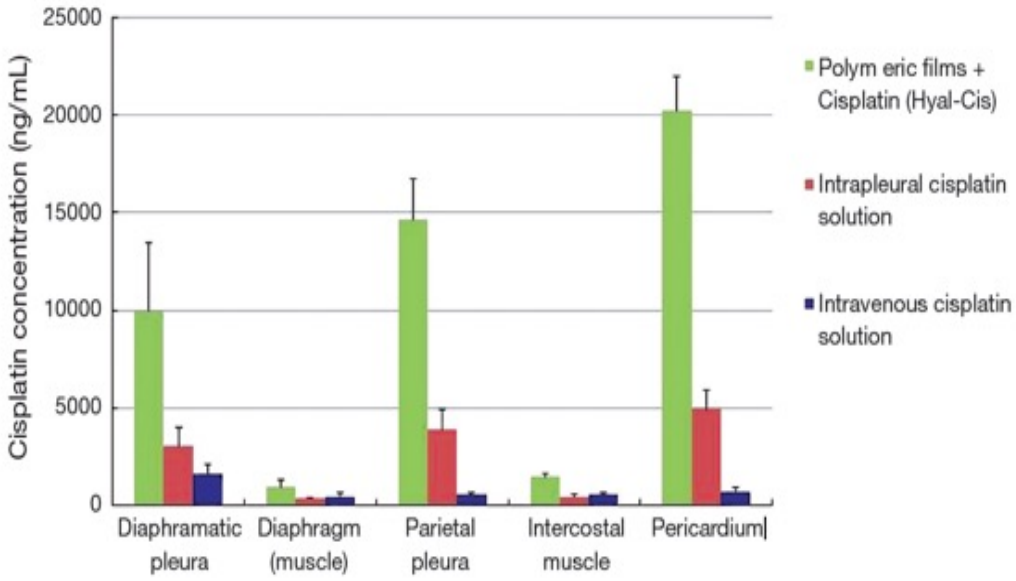
Primary objective: Plasmatic and tissue concentration of Cisplatin

Secondary objective: *Hematologic toxicity, Organ toxicity*

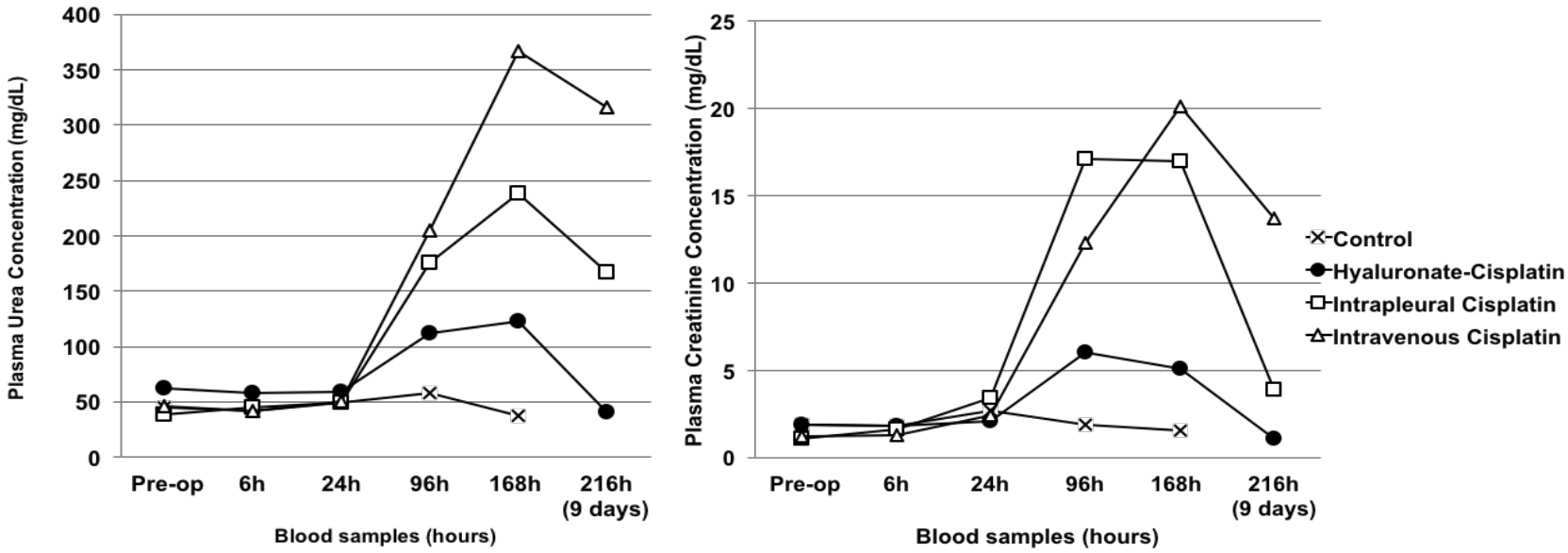
In vivo cisplatin tissue concentration

After Hyalcis administration cispla tin tissue concentrations were **hig h** for **diaphragm, pericardium, p arietal pleura and diaphragmati c pleura**.

Hyalcis films attain **higher local t issue concentrations** not only c ompared to the IV administration but also compared to the IP admi nistration of cisplatin solution.



Kidney toxicity biomarkers

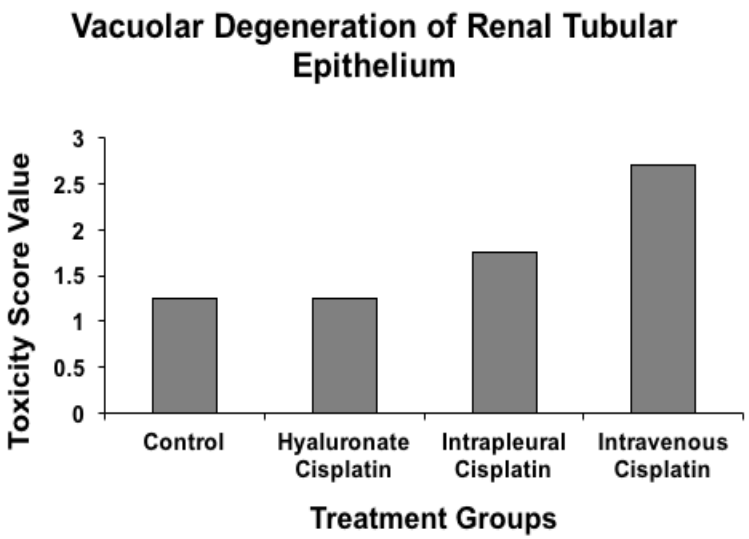


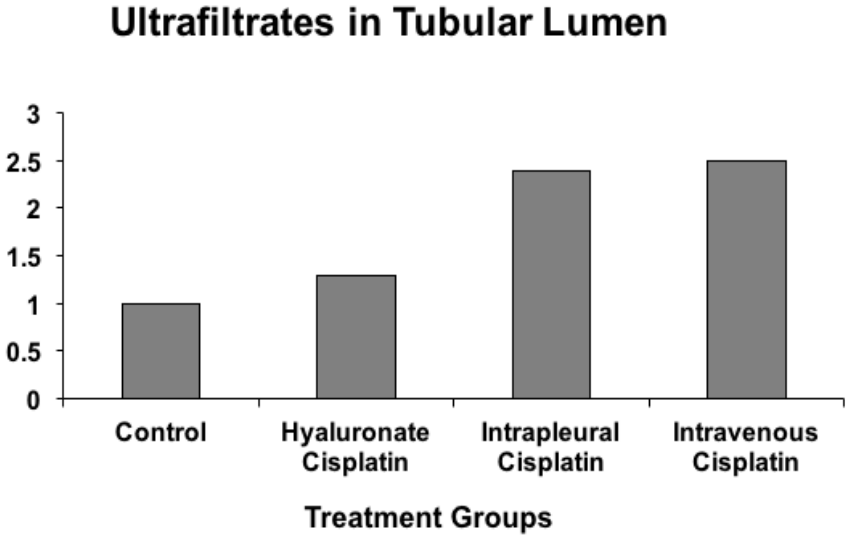
Nephrotoxicity is a typical toxicity of cisplatin. Two biomarkers of kidney toxicity were monitored during experiment, urea and creatinine.

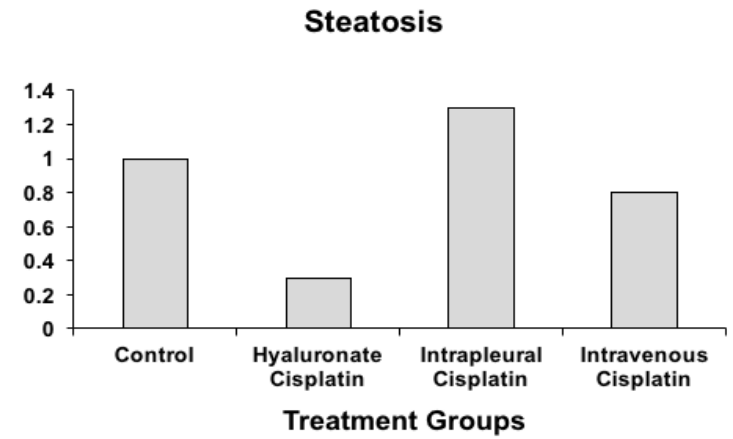
For both biomarkers the **plasma concentrations** obtained for the group treated with Hylacis were **lower** than those obtained for the groups treated with IV and IP cisplatin solutions.

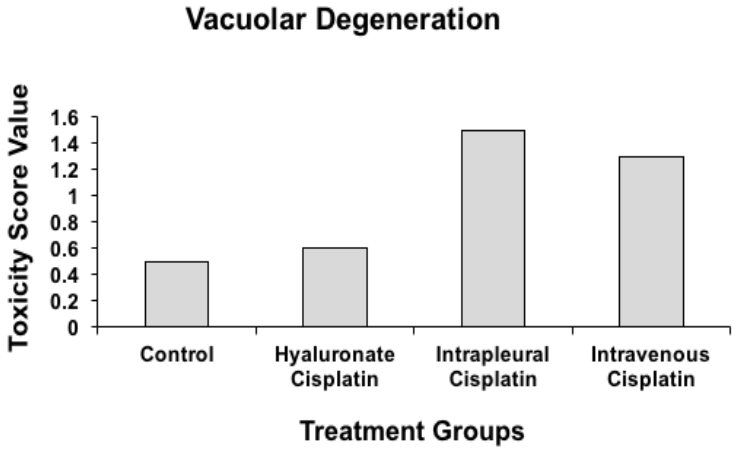
Histologic evaluation: kidney and liver

Toxicity score: 0 (no toxicity), 3 (severe anomalies)

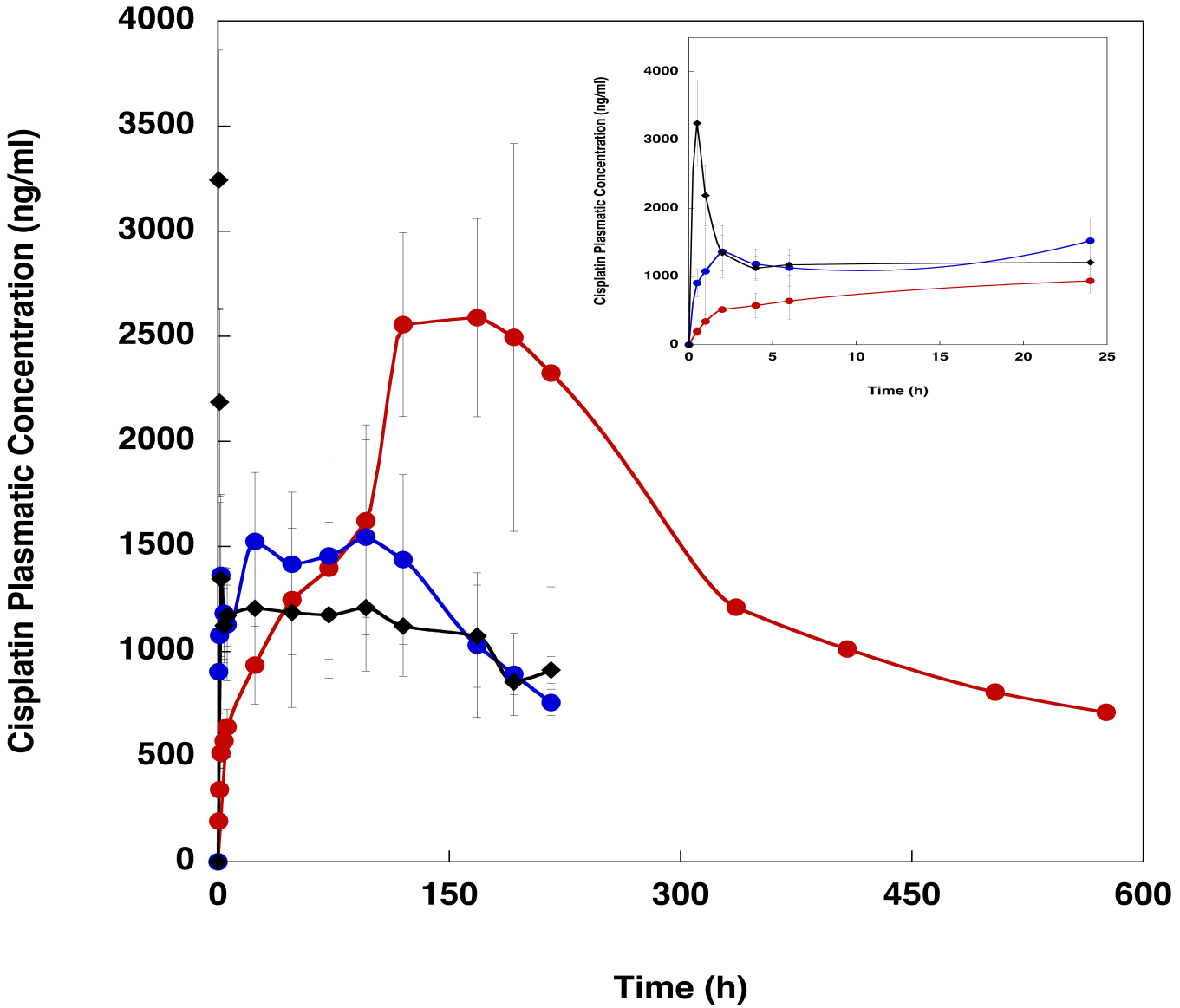








PLATIN PLASMATIC CONCENTRATION



BENEFITS OVER CURRENT THERAPIES

★ Unique dosage form for loco-regional chemotherapy

★Easy to handle and to apply to pleural surface *in vivo*

★ *In vitro* prolongation of drug release

★Sustained cisplatin plasma levels

★Elevated local cisplatin concentrations

★Suppress tumor in pleural recurrence rat model

★Remarkable tolerability with low kidney and liver toxicity in sheep model

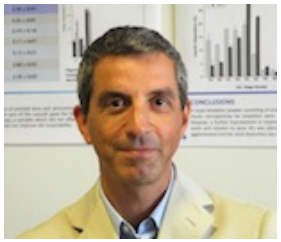
WHO WE ARE

The pharmaceutical technology researchers of PLU are world recognized and patent owners in medicines constructed on drug delivery technology

Prof.Paolo Colombo
CEO,Founder

Prof.Francesca Buttini
Founder

Anna Giulia Balducci
Founder



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Fabio Borella
Co-Founder
Marketing Manager

Laura Monica
Administrative
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“This film would improve the quality life of patients”

Luca Ampollini, Cardiothoracic Surgeon, University of Parma (IT)

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