



*Developing anti-cancer drugs: our mission, our work and our passion.*

# Ecrins Therapeutics

EuroQuity presentation, e-Pitch  
January, 2020



MD, PhD

# Team



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# Company governance

## Strategic Council



**Damien  
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PharmD, PhD, MBA, Head of Findmed (French technology transfer program). Ex TTO Institut Curie, ex Head of Marketing Oncology at Aventis, ex VC at Auriga Partners, ex CEO Novagali and Sepal Pharma



**Jean-Marc  
Herbert**

PhD, President of ARKELY-Consulting, Venture partner at GO Capital; ex Senior VP Discovery at Sanofi-Aventis Research. Member of several SAB of biotech companies

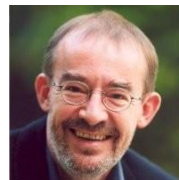
## Scientific Council



**Pr. Jacques  
Descotes**  
Toxicology



**Dr. Josiane  
Lemut**  
Chemistry,  
formulation,  
regulatory



**Dr. Gerald  
Thompson**  
Regulatory affaires  
Realtime Regulatory  
Ex-VP Sanofi



**Pr. Jean-Yves  
Blay**  
Clinical Oncology



**Jean-Jacques  
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Early Drug  
Development



**Dr. Claudine  
Vermot-Desroches**  
mABs  
development

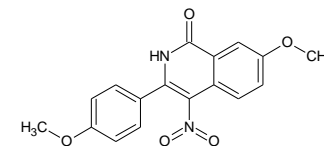


**Philippe Cassier,  
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Clinical Oncology

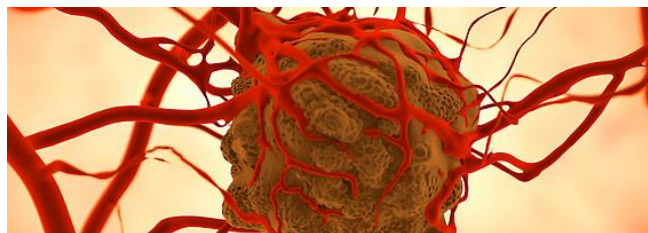


**Pr. Jean-Pierre  
Armand**  
Clinical Oncology

# Lead anti-cancer drug candidate ET-D5



First-in-class oral inhibitor of serine/ threonine protein phosphatase I (PP1)



Double anti-cancer activity

1. Anti-proliferative: stops tumour cell growth
2. Anti-vascular: destroys tumour neo-vascular structure

Patent WO2011/107709/A1 - 2011

Grenoble University/Institut Curie/CNRS

Granted: EU, USA, Japan, EAPO (Eurasia), Canada

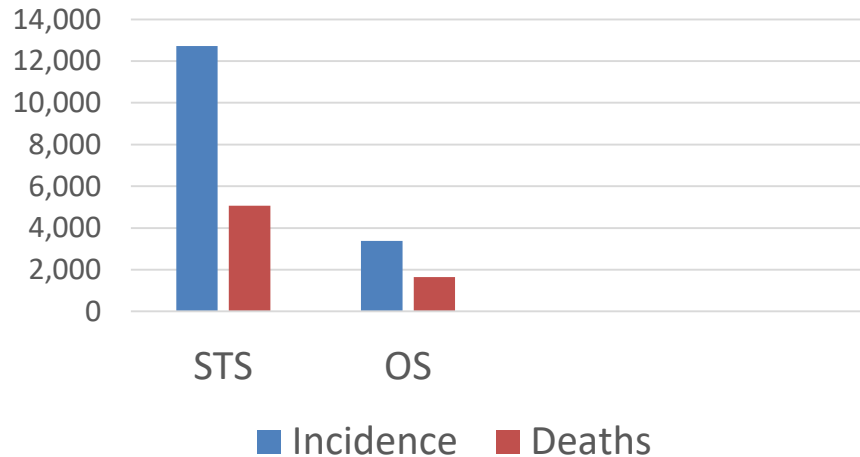
# Sarcomas, a gateway indication



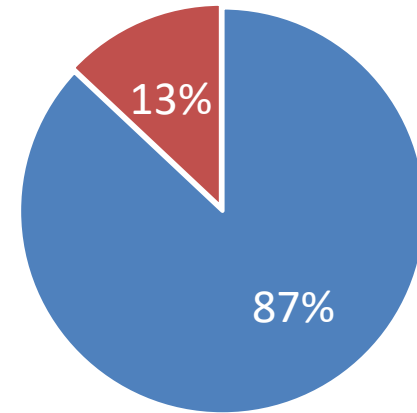
Clinical characteristics	Aggressive, highly vascularized cancers
Frequency	Orphan disease, 1% of all cancers. For osteosarcomas (OS) - up to 15% of all childhood cancers
Survival	for the metastatic osteosarcomas: 15-30% at 5 years for the metastatic soft-tissue sarcomas: 38% at 2 years
Chemotherapy standard of care	doxorubicin (DXR), cisplatin, ifosfamide- Limited efficacy, high toxicity
ET-D5 versus DXR	<i>In vitro</i> , on OS cells, ET-D5 is 3000 times more efficient than DXR
Putative biomarker expression	High, PP1 $\gamma$ isoform overexpressed in OS cells ( <a href="https://doi.org/10.1016/0304-3835(95)90150-7">doi.org/10.1016/0304-3835(95)90150-7</a> )
<i>In vivo</i> clinical efficacy	Translational clinical trial in dogs with spontaneous sarcomas is under way. <b>So far, 5/6 treated dogs have shown stable disease</b>
Alternative therapies	The most promising candidate, olaratumab (anti-PDGFR $\alpha$ ) of Ely, has just failed in confirmatory Phase III trial

# Sarcoma drugs market size

Epidemiology of sarcomas in the US (2017)



All sarcomas



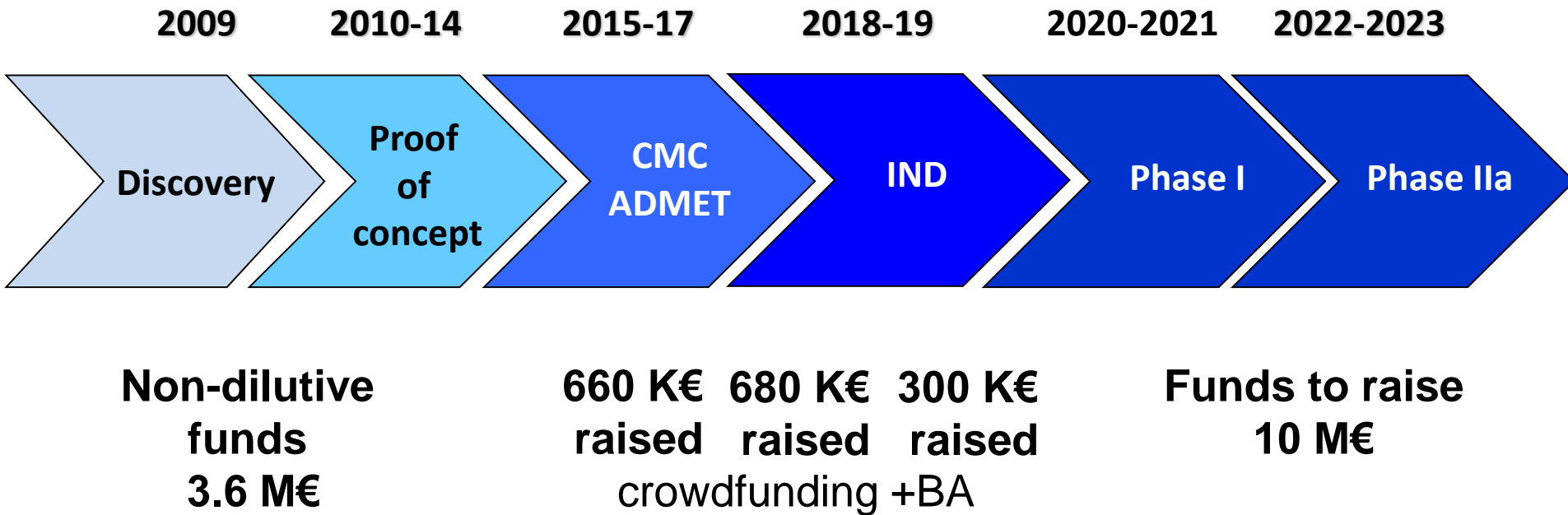
■ Soft tissue sarcomas ■ Osteosarcomas

- The global sarcoma drugs market size was \$703m in 2017 and will reach 1.2 bn in 2023 (CAGR of 8.5% in 2018-2023) – Grand View Research, Inc.
- The number of sarcoma patients in Europe is more than double than in the USA – 28,000 per year.
- Eli Lilly's olaratumab was granted by FDA accelerated approval in Oct 2016 for STS. Before losing market authorization in Jan 2019, olaratumab generated close to 1 bn in sales for this indication.
- Subject to successful FIH trial, ET-D5 could win a conditional market authorization in 2023 and generate \$300-400m per year

## Lead product ET-D5, stages of the project

Stage of development	
CMC, Formulation, Toxicology, Safety	✓
IND, Briefing Package, Investigator's Brochure, Clinical Protocol	✓
Pre-IND meeting application	✓
Written responses from the FDA – “no major issues”	✓
Phase I start	Q2, 2020

# ET-D5 development: Milestones and Finances














# Investment thesis

- The lead product ET-D5, is a first-in-class inhibitor of PP1 with a proven *in vitro* and *in vivo* anticancer activity.
- ET-D5 is at the door of the first-in-human clinical trial of Phase I/IIa targeting sarcomas, a relatively rare subgroup of cancers for which currently there is no efficient treatment.
- ET-D5 has already shown preliminary clinical efficacy in dogs suffering from spontaneous sarcomas.
- ECRINS submitted to FDA a pre-IND package and obtained (June 2019) a positive feedback from the Agency. FDA validated the CMC and safety/toxicology results.
- The Phase I/IIa clinical trial in sarcoma indication is scheduled for Q2 2020 and will take up to 36 mo in Dana-Farber Cancer Institute (US) and Royal Melbourne Hospital (AU).
- Realistic estimates suggest that in case of success ET-D5 will capture a large share of the sarcoma market with immediate (after Phase IIa) net sales of up to \$300-400m.
- ECRINS plans for an industrial exit after the completion of the Phase IIa trial of ET-D5.  
=> **Relatively short investment horizon (40 months)**

# Recent exits of VCs-backed biotechs in oncology (small molecules)

Biotech		Deal	Acquired by
IFM Therapeutics		\$1.3 bn	BMS
Acetylon		\$1.7 bn	Celgene
Nimbus Apollo		\$1.2 bn	Gilead
Acerta Pharma		\$4.0 bn	Astra Zeneca
Impact Biomedicines		\$7 bn	Celgene
Flexus Biosciences		\$1.25 bn	BMS
Blueprint Medicines		\$0.9 bn	Roche
Puma Biotechnology		\$3.6 bn	IPO
Seragon Pharmaceuticals		\$1.7 bn	Genentech

## Contact details

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# Pipeline

## Stage of development

### Asset / Indication

### Target

### Discovery

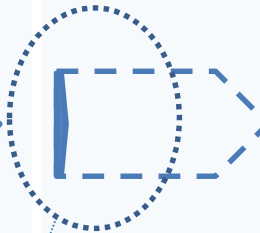
### ADMET

### Phase I/IIa

### Exit/use strategy

**ET-D5**  
**Human oncology**  
Sarcomas (gateway)  
Other solid tumors

PP1



Major value-creation step  
for ET-D5  
Go/NoGo (2023)  
after completion of Phase IIa

**ET-D5**  
**Translational oncology**  
(Sarcomas, solid tumors  
in dogs)

PP1



Results will help to focus  
on “best” indications for  
human clinical trial.  
Possibility to sell the asset  
for vet. applications (2020)

**Small molecule,**  
oncology

first-in-class,  
undisclosed



Patent expected in 2021

**Therapeutic mAb,**  
oncology

first-in-class,  
undisclosed

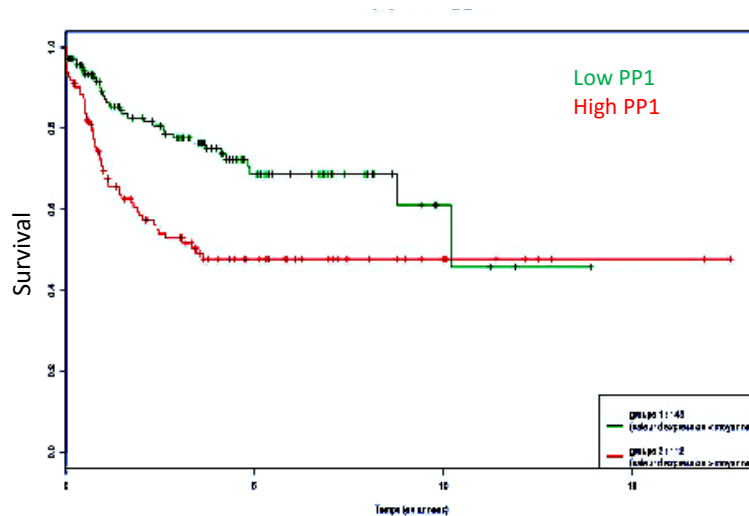


Patent expected in 2021

Pre-IND application (June 2019) – “no major issues”  
Investigator’s brochure ready  
Clinical protocol ready

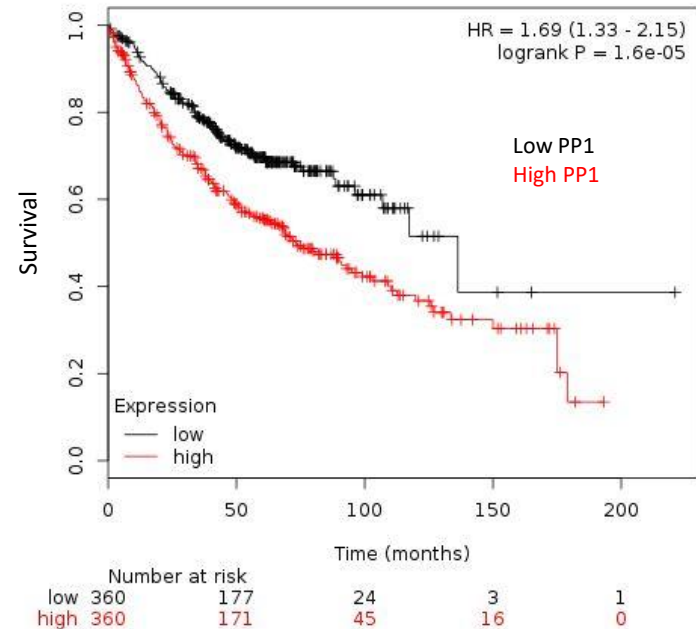
# PP1, a previously unexplored cancer target

## Sarcomas



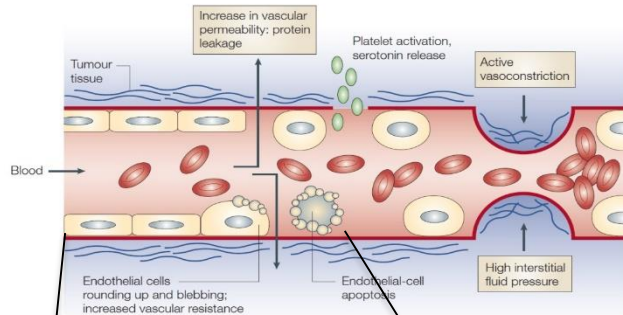
Kaplan-Meier analysis shows that PP1 over-expression correlates with early death in sarcoma and lung cancer patients, among others.

## Lung adenocarcinomas

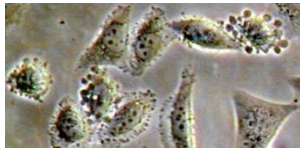


# Double activity of ET-D5

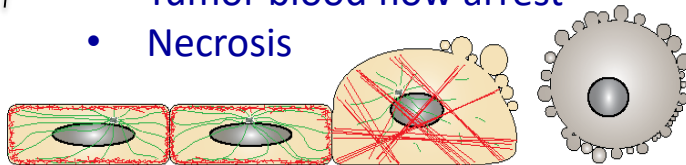
## On tumor endothelial cells



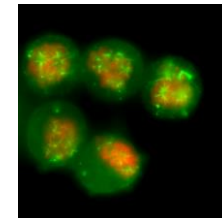
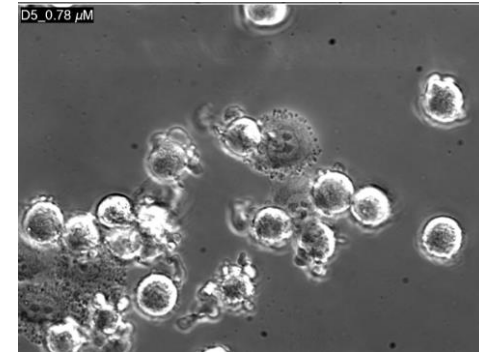
Tozer: Nature reviews



- Microtubule depolymerization
- Actin reorganization
- Blebbing
- Apoptosis
- Tumor blood flow arrest
- Necrosis



## On tumor cells

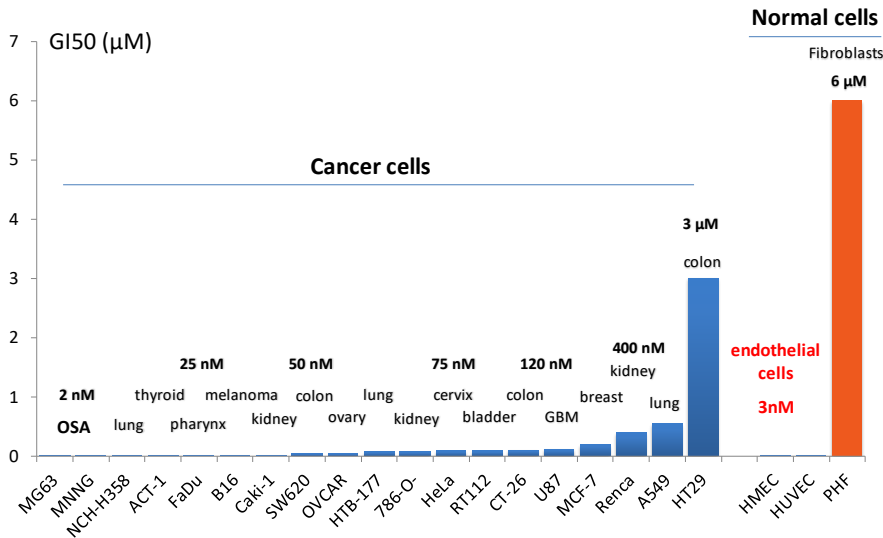


- Microtubule depolymerization
- Blebbing
- Cell cycle arrest
- Tumor growth arrest and/or
- Tumor cell death

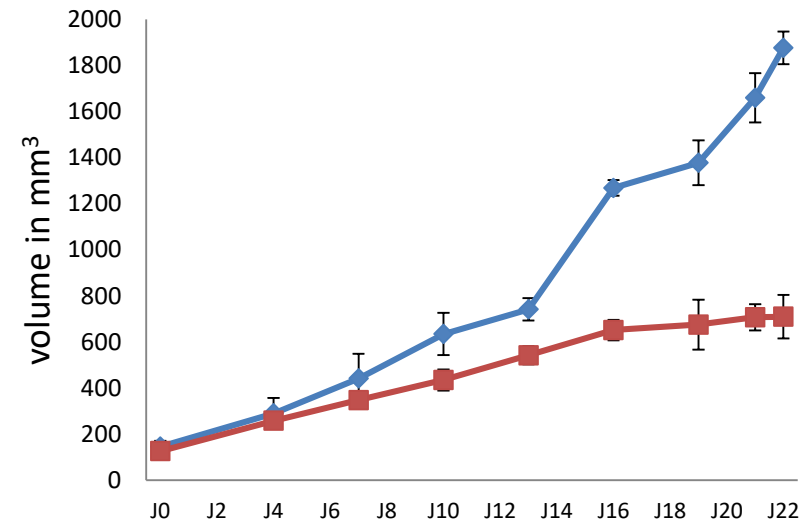
# *In vitro* and *in vivo* efficacy of ET-D5



## GI50, anti-proliferation activity of ET-D5 on a panel of cancer and normal cells



## Anti-tumor activity of oral ET-D5 in a mouse xenograft model (NSCLC, HTB-177)



- Most of cancer cells are inhibited in a low nanomolar range
- Normal cells are very resistant to ET-D5 (ther. index)
- Endothelial cells are very sensitive to ET-D5 (anti-vascular)
- In the human lung cancer model, ET-D5 produces an ILS of 64%
- NB: non-formulated API

## Regulatory toxicology studies -SUMMARY

### Toxicology study plan

1. Genotoxicity studies (non-GLP)
2. 4-wk GLP-toxicity study in rats (plus 2-wk treatment-free period)
3. 4-wk GLP-toxicity study in dogs (plus 2-wk treatment-free period)
4. Safety battery (heart telemetry, respiration, CNS)

### Results ( NO SAFETY ISSUES ! )

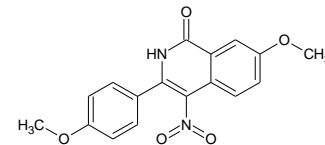
Genotox	Probably NOT-mutagenic for humans, caution advised
Tox in rats	No clinical signs; plasma exposure $\nearrow$ with dose; higher exposure in females; stable plasma exposure from D1 to D28; <b>NOAEL 1000 mg/kg</b>
Tox in dogs	Reversible pseudoallergic reactions starting 300 mg/kg; <b>NOAEL 100mg/kg</b>

### Conclusions:

- Relatively low toxicity in both species studied. No hematological or GI toxicities! Toxicology profile resembles that of targeted therapies, rather than « traditional » chemotherapies.
- Circulating levels of ET-D5 were relatively low in dogs and relatively high in rats:  
 $C_{\max} = 8,035 \text{ ng/mL}$   
 $AUC_{(0-t)} = 74,380 \text{ ng}\cdot\text{h/mL}$   
Circulating levels in humans are likely to be similar or higher than those in rats.



## Safety/Toxicity profile of ET-D5: competitive advantage over existing therapies



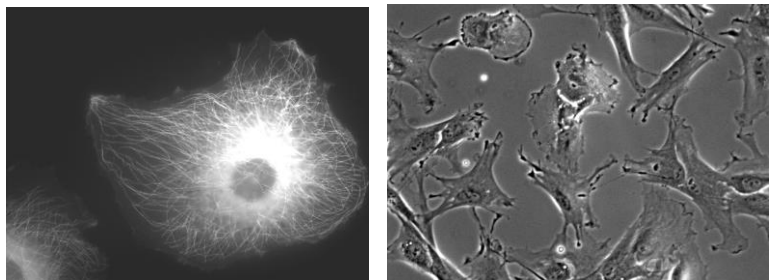
In two different animal species ET-D5 has shown NO safety issues and an excellent toxicity profile (NOAEL in rats 1000 mg/kg ; NOAEL in dogs 100 mg/kg)

Should this toxicity profile of ET-D5 be confirmed in FIH clinical trial, it will:

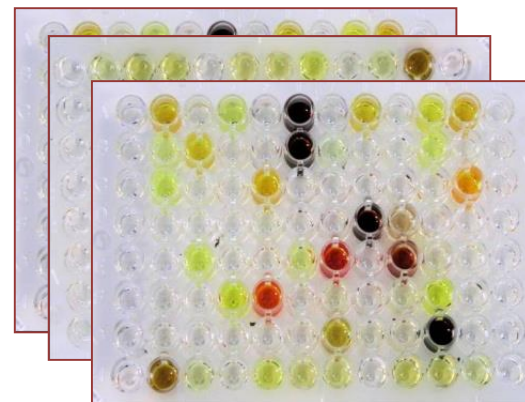
- Allow using the drug in monotherapy at a dose necessary to achieve a clinical benefit.
- Allow using the drug in combination therapy with existing anti-cancer drugs, including other anti-vascular drugs and immunotherapies.

Overlapping safety/toxicity problems are **the reason** why many approved drugs cannot be combined or are used at a dose too low to unleash their full potential (e.g. bevacizumab + Tyr kinase inhibitors).

# Technology: high content phenotypic screening to identify bioactive molecules



Screening on live cells: primary or cancer cells, wild-type or modified to represent a desired pathological state

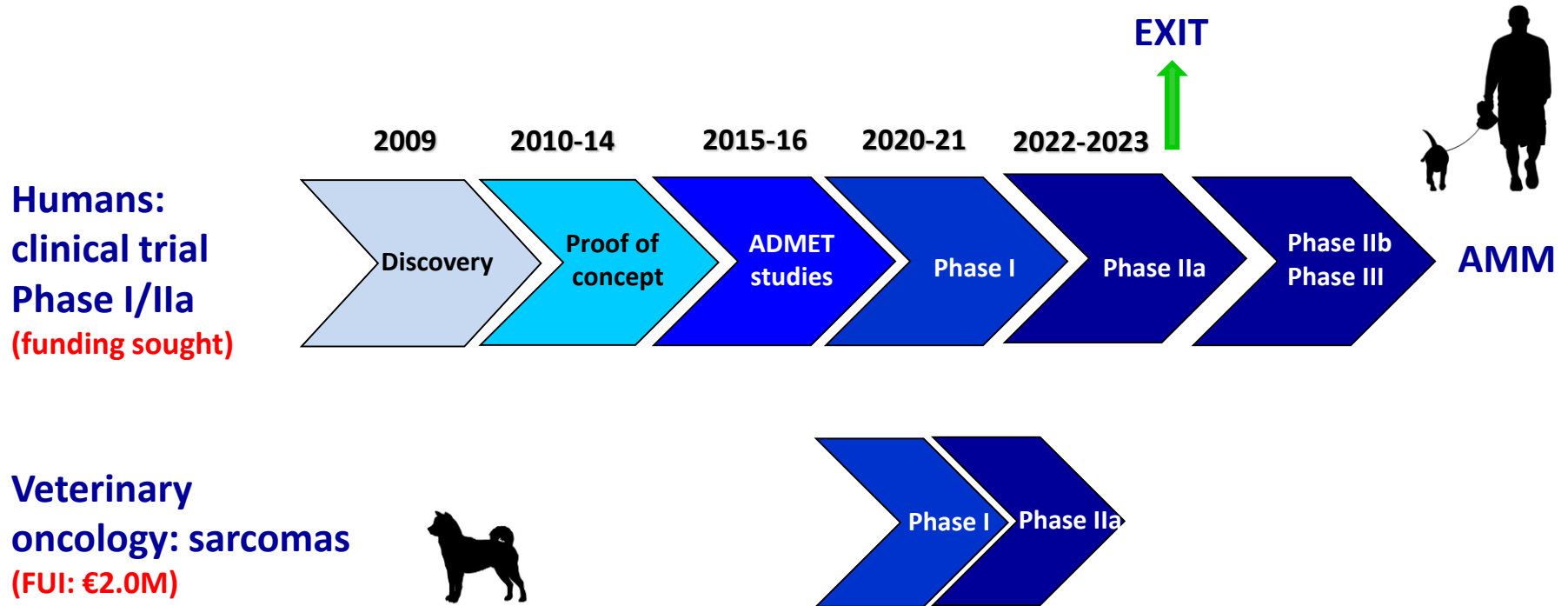


- 10, 000 small molecules (ChemDiv)
- 2, 000 plant extracts (Pierre Fabre)
- Custom-made mABs

## Deliverables:

1. Identification of drugs, producing (restoring) a desired phenotype
2. Identification of the target

# Translational oncology: perfect animal model to focus on responder indication (s)



Clinical trial is under way; six animals already dosed - early evidence of efficacy without SAEs

- **Goal: proof of concept, ET-D5 for sarcoma treatment**
- **Method: clinical trial in dogs with spontaneous sarcomas**

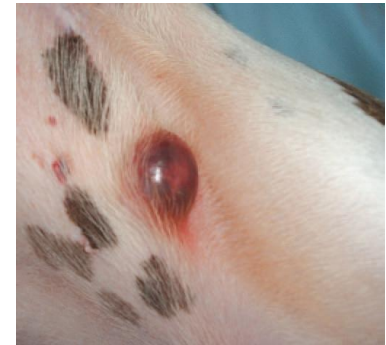
Why a canine clinical trial? Sarcomas are rare in humans (1% of all cancers), but frequent in dogs (15%)



**High grade soft-tissue sarcomas**



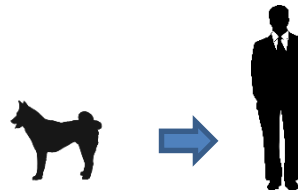
**Osteosarcomas**



**Hemangiosarcomas**

### Expected results:

- PdC of ET-D5
- Translation into human clinic
- Biomarkers validation



# Translational oncology: ET-D5 trial in canine sarcoma model

**Dose escalation Phase I clinical trial, aiming to define RD2P of ET-D5, in dogs with spontaneous sarcomas, non-operated and amenable to evaluation according to RECIST**

## **Phase I clinical protocol**

- Dose escalation (12 pts) + extension cohort (3 pts)
- 5 dose levels: 100, 200, 400 and 600mg/kg (28 days administration)

## **TRIAL OBJECTIVES**

- 1. Determine DLT and RD2P**
  - 2. Determine safety profile of ET-D5**
  - 3. Evaluate the PK and tumor response parameters according to RECIST 1.0, PD**
- pK: 7 blood samples over 24h
  - Contrast enhanced perfusion CT (tumor vascularisation on D0, D14, D28 and D56)
  - Anti-tumor activity according to RECIST criteria, by whole body CT (D0, D28 and D56)
  - PD: histology analysis + immunoblotting (p-MLC, PP1...) on biopsy samples: D0, D28, D56
- 
- First recruitment: July 2018

## Efficacy statement – after only six animal patients treated

Pt	Dose	Indication	Safety	RECIST Evaluation	Effect on Tumor vascularization	Necrosis	New metastasis
01-01	100	Myxosarcoma	OK	SD	Yes	Yes	No
02-01	200	Fibrosarcoma	OK	SD	Yes	Yes	No
02-02	200	STS	AE3	SD	Yes	Yes	No
02-03	200	Leiomyo-sarcoma	OK	PD	No	No	Yes
02-05	200	Rhabdomyo-sarcoma	OK	SD	NE	NE	No
02-06	200	Liposarcoma	OK	SD	NE	NE	No







- Next dose levels : 400 and 600 mg/kg
- Analysis of the correlation with biomarker #1 under way (PD)
- Non-responding patient 02-02 showed a very low level of plasma ET-D5

## Efficacy statement (2)

### Results

- Stabilization of the disease for 5 patients out of 6 during the treatment
- Anti-vascular effect observed in 3 dogs out of 4 (tumoral necrosis)
- Constant ET-D5 plasma exposure between Day 0 and day 28
- ET-D5 plasma exposure higher than during TK study in beagle dogs
- No major toxicity except one reversible Grade 3 AE
- Progression of disease in some pts AFTER the end of 28-days treatment cycle
- No new metastasis in ALL pts with SD
- One non-responder (1/6) with PD and new metastasis (low circulating levels in this dog)

# Human oncology: target product profile

Attribute	Target	State
<b>Clinical pharmacology and PK</b>	<ul style="list-style-type: none"> <li>Oral administration</li> <li>Safety and PK profiles compatible with a daily dosing</li> </ul>	 
<b>Indication(s) and usage</b>	Aggressive, vascularized tumors: sarcomas (gateway indication*), followed by kidney, colon, lung, liver cancers, expressing relevant biomarkers	
<b>Primary efficacy endpoints</b>	<ul style="list-style-type: none"> <li>Tumor regression in monotherapy</li> <li>Tumor regression in combination therapy; improved survival</li> </ul>	Planned
<b>Secondary efficacy endpoints</b>	<ul style="list-style-type: none"> <li>Progression-free survival</li> <li>Objective response rate (RECIST v. 1.1)</li> </ul>	Planned Planned (stable disease in dogs)
<b>Expected safety and tolerability outcomes</b>	<ul style="list-style-type: none"> <li>Rare AE (rare hypersensitivity reactions in dogs);</li> <li>No cardiovascular AEs in tox studies</li> </ul>	
<b>Dosage and regimen</b>	Oral nanosuspension or oral solid form; QD or BID	
<b>Stability</b>	At least 36 months for the API	



# First-in-human clinical trial – protocol synopsis

Title	A Phase I, open-label, multicenter trial using a mCRM-based design with an expansion cohort to define the MTD and the RP2D of ET-D5 administered orally, as single agent, in advanced cancer patients
Study duration	36 months
Population	<ul style="list-style-type: none"><li>• <b>Phase I:</b> 30 pts with advanced solid tumors (osteosarcoma, STS, GIST, kidney cancer, ATC, HCC, colon, lung)</li><li>• <b>Phase IIa:</b> up to 48 pts with advanced solid tumors</li></ul>
Objectives Phase I	<ul style="list-style-type: none"><li>• <b>Primary:</b> MTD, RP2D</li><li>• <b>Secondary:</b> safety, tox profile, PK, prelim. evidence of activity</li></ul>
Objectives Phase IIa	<ul style="list-style-type: none"><li>• <b>Primary:</b> tumor response rate</li><li>• <b>Secondary:</b> OS, PFS, confirm RP2D, additional tox data, tumor parameters associated with response and outcome</li></ul>
Exploratory objectives (Ph I/IIa)	<ul style="list-style-type: none"><li>• Variation in tumor blood perfusion (CT/DCE-MRI/ultrasound), non-invasive biomarker.</li><li>• Assessing PD activity in tumors; identify additional biomarkers</li></ul>
Study design	<ul style="list-style-type: none"><li>• <b>Phase I:</b> dose-escalation until DLT; mCRM model driven</li><li>• <b>Phase IIa:</b> expansion cohort to evaluate TRR</li></ul>
Administration	Oral form; 4 weeks

# Clinical trial Phase I/IIa – major value creating step



**Dr Suzanne  
GEORGE**

**USA**



Pr. Jean-Yves Blay

**Pr. Jean-Yves  
Blay**



**Dr. Philippe  
Cassier**



**France  
EUROPE**

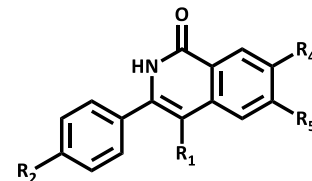


**Dr. Jayesh  
Desai**



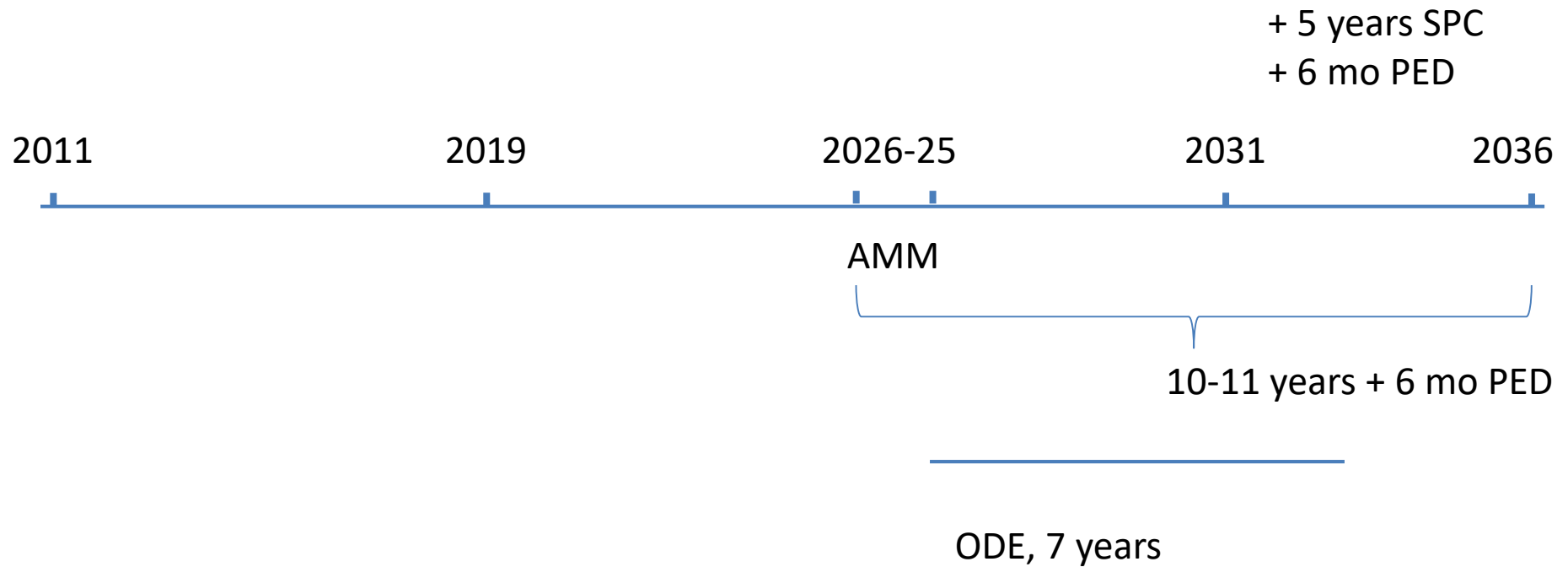
**The Royal  
Melbourne Hospital**

**Australia**

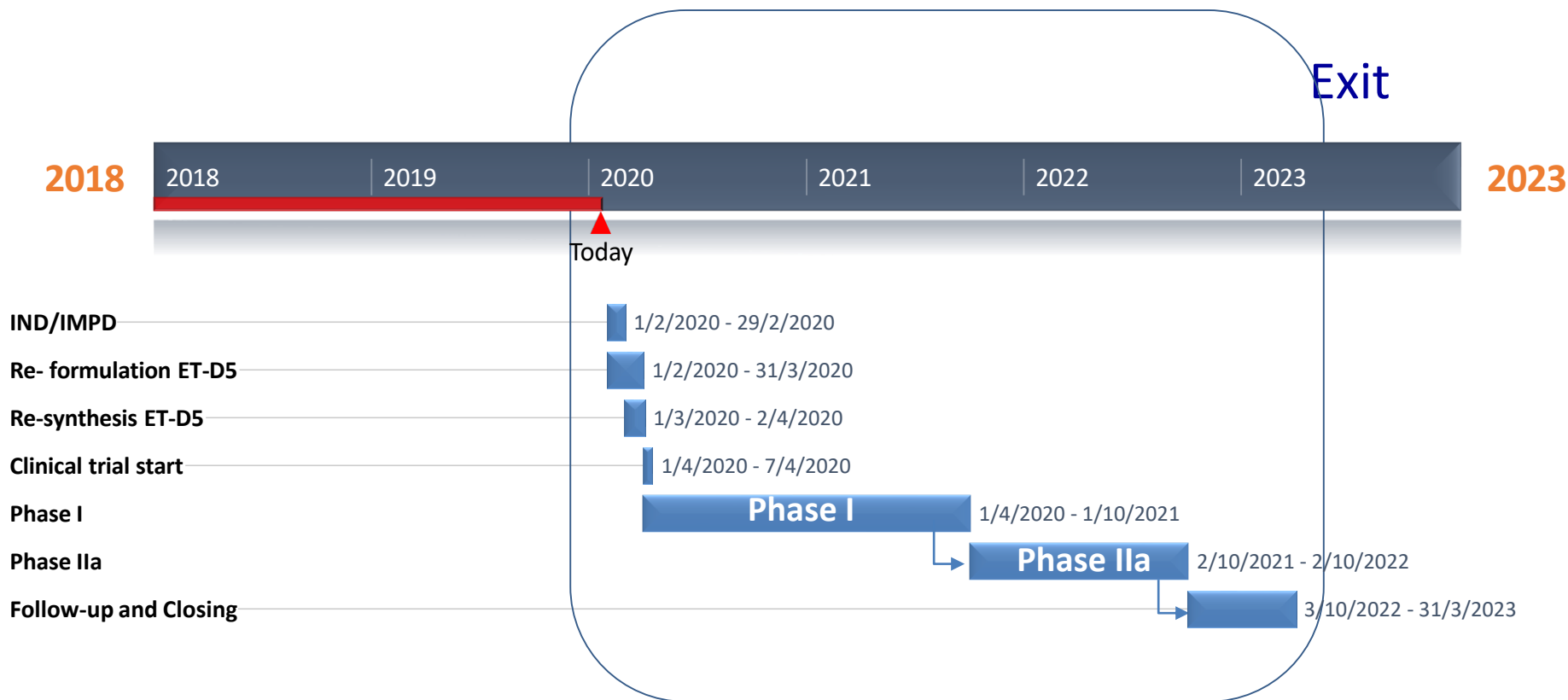


- Patent WO2011/107709/A1 - 2011  
Grenoble University/Institut Curie/CNRS  
Granted: EU, USA, Japan, EAPO (Eurasia), Canada
- World-wide exclusive license for Ecrins Therapeutics, right to sublicense, direct control over patent attorneys
- Further protection expected: ET-D5 and companion test (biomarkers and combination therapy)
- SPC and orphan designation possible  
(7 more years in the USA and 10 years in the EU)

# IP protection strategy – ET-D5 patent



# ET-D5 development plan



# Budget

		Y1 (2020)	Y2(2021)	Y3(2022)	Y4 (2023)
Internal costs	€	429,764	778,497	808,707	856,983
R&D		38,438	41,338	44,525	48,029
Ousourcing academic		10,000	11,000	12,100	13,310
Rent		50,977	53,426	55,997	58,697
General expenses		238,196	248,753	286,252	295,883
Equipments		10,000	10,000	10,000	10,000
Salaries		739,835	776,349	814,689	854,946
Taxes		7,098	7,558	5,000	5,000
CROs		2,188,734	1,730,880	1,280,880	188,480
Financial charges		273,830	209,070	165,967	163,158
Total		3,557,109	3,088,374	2,675,411	1,637,503
Total	10,958,396				

# Highlights

- First-in-class compound with interesting follow-up programs.
- **Canine spontaneous cancer model shows efficacy in dogs with sarcomas.**
- Experienced and highly motivated team + large network of partners.
- CMC and ADMET completed -> no safety issues !
- Excellent safety and toxicology profile .
- Pre-IND submission -> positive feedback from the FDA.
- Potential biomarkers identified.
- Entry indication in humans: sarcomas (no efficient therapy available).
- Follow-up indications (current therapies): lung (targeted and Pt-based, immuno-therapies), colon (5-FU, Pt-based, Irinotecan, anti-VEGF and anti-EGF), HCC (Sorafenib), thyroid (Sorafenib, Lenvatinib).
- First-in-human trial: clinical centers, CROs and PI identified

## Rational for the future use of ET-D5 in combination with anti-vascular therapy

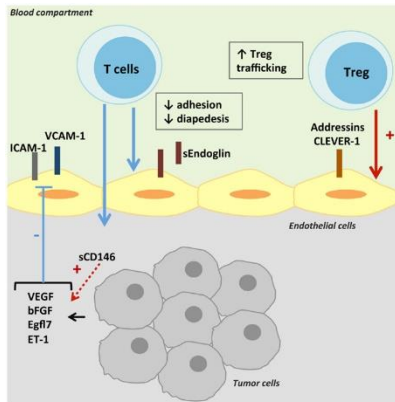
### ET-D5 is likely to be used in aggressive, vascularized cancers:

- Sarcomas
- NSCLC (lung cancer)
- Kidney cancer,
- Ovarian cancer,
- HCC etc...

### Putative targets for the combination therapy:

- Anti-VEGF MABs : Avastin (Roche), Mvasi (Amgen), Bevacizumab
- Anti-VEGF small molecules: Sutent (Pfizer), Pazopanib (GSK), Sorafenib (Bayer)

## Rational for the future use of ET-D5 in combination with immunotherapy



### Observation:

- Tumor vascular endothelial protect tumor cells from immunotherapy (barrier function). Targeting tumor endothelial cells with anti-vascular drugs improves the efficacy of immunotherapy.

### Hypothesis:

- ET-D5 should enhance the potential of existing cell-based and Ig-based immunotherapies

### Solution:

- Proof-of-concept experiments scheduled (CD3+ tumor infiltration)

L. Mauge *et al.* Front. Oncol. 2014



# Indications , where anti-vascular drugs have been approved by FDA

Drug	Trade name	1 <sup>st</sup> line indications	2 <sup>d</sup> line indications
<a href="#"><u>Axitinib</u></a>	<a href="#"><u>(Inlyta®)</u></a>		RCC
<a href="#"><u>Bevacizumab</u></a>	<a href="#"><u>(Avastin®)</u></a>	Colon, NSCLC, RCC, cervical cancer	Colon, GBM, ovarian cancer
<a href="#"><u>Cabozantinib</u></a>	<a href="#"><u>(Cometriq®)</u></a>	Thyroid cancer	RCC
<a href="#"><u>Everolimus</u></a>	<a href="#"><u>(Afinitor®)</u></a>	PNET, NET, GI, NSCLC	RCC, HER2(-) breast cancer
<a href="#"><u>Lenalidomide</u></a>	<a href="#"><u>(Revlimid®)</u></a>		Myeloma, mantle-cell lymphoma
<a href="#"><u>Lenvatinib mesylate</u></a>	<a href="#"><u>(Lenvima®)</u></a>	Thyroid cancer	RCC
<a href="#"><u>Pazopanib</u></a>	<a href="#"><u>(Votrient®)</u></a>	RCC	STS
<a href="#"><u>Ramucirumab</u></a>	<a href="#"><u>(Cyramza®)</u></a>		Colon, gastric adenocarcinoma, NSCLC
<a href="#"><u>Regorafenib</u></a>	<a href="#"><u>(Stivarga®)</u></a>		Colon, GIST, HCC
<a href="#"><u>Sorafenib</u></a>	<a href="#"><u>(Nexavar®)</u></a>	RCC, HCC	
<a href="#"><u>Sunitinib</u></a>	<a href="#"><u>(Sutent®)</u></a>	RCC, PNET	GIST
<a href="#"><u>Thalidomide</u></a>	<a href="#"><u>(Synovir, Thalomid®)</u></a>	Myeloma	
<a href="#"><u>Vandetanib</u></a>	<a href="#"><u>(Caprelsa®)</u></a>	Thyroid cancer	
<a href="#"><u>Ziv-aflibercept</u></a>	<a href="#"><u>(Zaltrap®)</u></a>		Colon cancer

## Most likely indications for ET-D5: aggressive, highly vascularized cancers

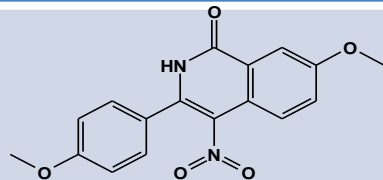
Based on preclinical Ecrins Therapeutics results	Based on existing clinical experience with anti-vascular drugs	Consensus most likely indications
Colon (xenograft necrosis)	Colon	<b>Colon</b>
RCC (xenograft necrosis)	RCC	<b>RCC</b>
Sarcomas (necrosis, cell death, stable disease in treated dogs)	Sarcomas	<b>Sarcomas</b>
NSCLC (tumour growth delay, xenograft necrosis)	NSCLC	<b>NSCLC</b>
Thyroid (xenograft necrosis, neovessels death)	Thyroid	<b>Thyroid</b>
Not tested	HCC	NA
Not tested	GIST	NA

## Safety and toxicity profiles of already approved anti-vascular drugs

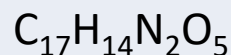
Drug	Trade name	Adverse effects
<a href="#"><u>Axitinib</u></a>	<a href="#"><u>(Inlyta®)</u></a>	Cardiovascular, thrombosis, bleeding
<a href="#"><u>Bevacizumab</u></a>	<a href="#"><u>(Avastin®)</u></a>	GI perforations, bleeding, thrombosis, bleeding, hypertension
<a href="#"><u>Cabozantinib</u></a>	<a href="#"><u>(Cometriq®)</u></a>	Hand-and-foot syndrome, diarrhea, hypertension, bleeding
<a href="#"><u>Everolimus</u></a>	<a href="#"><u>(Afinitor®)</u></a>	Asthenia, GI AE, vomiting, infections, myelosuppression
<a href="#"><u>Lenalidomide</u></a>	<a href="#"><u>(Revlimid®)</u></a>	Teratogenicity, myelosuppression, thrombosis, vomiting, diarrhea, neurotoxic effects
<a href="#"><u>Lenvatinib mesylate</u></a>	<a href="#"><u>(Lenvima®)</u></a>	Hypertension, vomiting, diarrhea, bleeding, thrombosis, hepatotoxicity, nephrotoxicity
<a href="#"><u>Pazopanib</u></a>	<a href="#"><u>(Votrient®)</u></a>	Hypertension, vomiting, diarrhea, asthenia, bleeding, thrombosis myelosuppression
<a href="#"><u>Ramucirumab</u></a>	<a href="#"><u>(Cyramza®)</u></a>	Hypertension, bleeding, fatigue, vomiting, diarrhea, GI perforation
<a href="#"><u>Regorafenib</u></a>	<a href="#"><u>(Stivarga®)</u></a>	Hypertension, hand-and-foot syndrome, bleeding, hepatotoxicity
<a href="#"><u>Sorafenib</u></a>	<a href="#"><u>(Nexavar®)</u></a>	Hypertension, hand-and-foot syndrome, bleeding, wound healing pbs
<a href="#"><u>Sunitinib</u></a>	<a href="#"><u>(Sutent®)</u></a>	Hypertension, skin rash, bleeding, asthenia, diarrhea, myelosuppression
<a href="#"><u>Thalidomide</u></a>	<a href="#"><u>(Synovir, Thalomid®)</u></a>	Teratogenicity, fatigue, peripheral neuropathy, skin toxicity
<a href="#"><u>Vandetanib</u></a>	<a href="#"><u>(Caprelsa®)</u></a>	Skin reactions, diarrhea, fatigue, hypertension, bleeding
<a href="#"><u>Ziv-aflibercept</u></a>	<a href="#"><u>(Zaltrap®)</u></a>	Hypertension, GI perforations, bleeding, thrombosis, myelosuppression

## Structure

## Structural formula



## Molecular formula



## Molecular weight

326.31 g/mol

## Stability

## Condition

## Result

ET-D5  
Drug  
Substance

25°C/60%RH

Stable 3 years  
(still ongoing)

30°C/65%RH

Stable 12 mths

40°C/75%RH

Stable 6 mths

5°C ± 3°C

Stable 2 years  
(still ongoing)ET-D5  
Drug  
Product

25°C/60%RH

Stable 6 mths

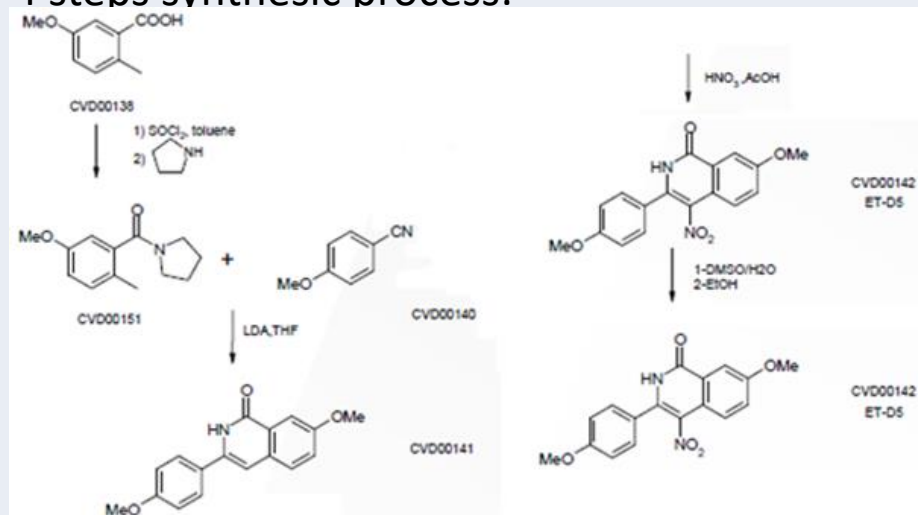
2-8°C

Stable 6 mths

## Manufacturing

## ET-D5 Drug Substance

4 steps synthetic process:



Purity 99.9%

## ET-D5 Drug Product

Nanosuspension (d50~140nm)

Formula: ET-D5 (20%), PVP (3%), DOSS (0.5%), Tween80 (0.5%), Purified water (76%)

# Renal cell carcinoma, likely follow-up indication



Clinical characteristics	Agressive, highly vascularized cancer
Frequency	12 <sup>th</sup> most frequent cancer. 340 000 new cases annually
Survival at 5 years	53% and 8% for pts diagnosed at stage III and IV, respectively
Chemotherapy options	IL-2, IFN- $\alpha$ , Bevacizumab, Sutent, Pazopanib, Sorafenib, Everolimus, Temsirolimus, Lenvatinib, Axitinib, Nivolumab, Cabozantinib ... many options, but <b>LIMITED EFFICACY</b>
ET-D5	<i>In vitro</i> , on RCC cells, ET-D5 kills cancer cells at 50-400 nM