PLASFER

PLATELET TRANSFER TECNOLOGY

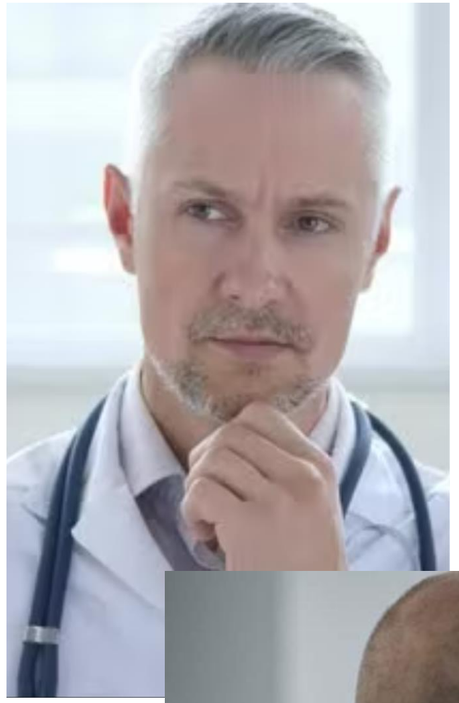
Unlocking the Power of Platelets

October -2023

Plasfer srl

Cancer is a Killer

Advanced/Metastatic Cancers are responsible for ~90% of cancer deaths



Cancer
is the **second** leading cause of preventable **death** globally

In 2018 -
World Wide
17m patients
9.6m deaths
1 in 6 deaths[1,2]

US
1.7m patients
600k deaths [3]
1 in 3 lifetime chance of developing cancer[4]

Cancer

Five year patient survival rates

Origin	Primary%	Metastasis%
Breast	98.0	26.7
Colon/Rectum	89.8	10.3
Pancreas	20.3	1.7
Kidney	89.6	9.5
Larynx	81.1	23.9
Liver	22.3	2.8
Lung/Bronchus	49.1	3.0
Melanoma of skin	98.5	15.3
Ovary	92.4	29.8

American Cancer Society, Cancer Facts & Figures **2013**

1 https://www.who.int/news-room/fact-sheets/detail/cancer
2 https://www.cancer.org/research/cancer-facts-statistics/global.html
3 https://seer.cancer.gov/statfacts/html/all.html
4 https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/annual-cancer-facts-and-figures/2019/cancer-statistics-presentation-2019.pptx

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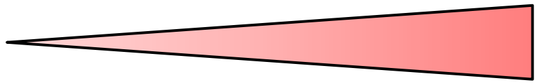
Platelets – WHY?
Platelet/Tumor Interactions are Critical for Advanced, Metastatic Cancer

Tumor Cell/Platelets Interactions Increase With Time/Age

Benign

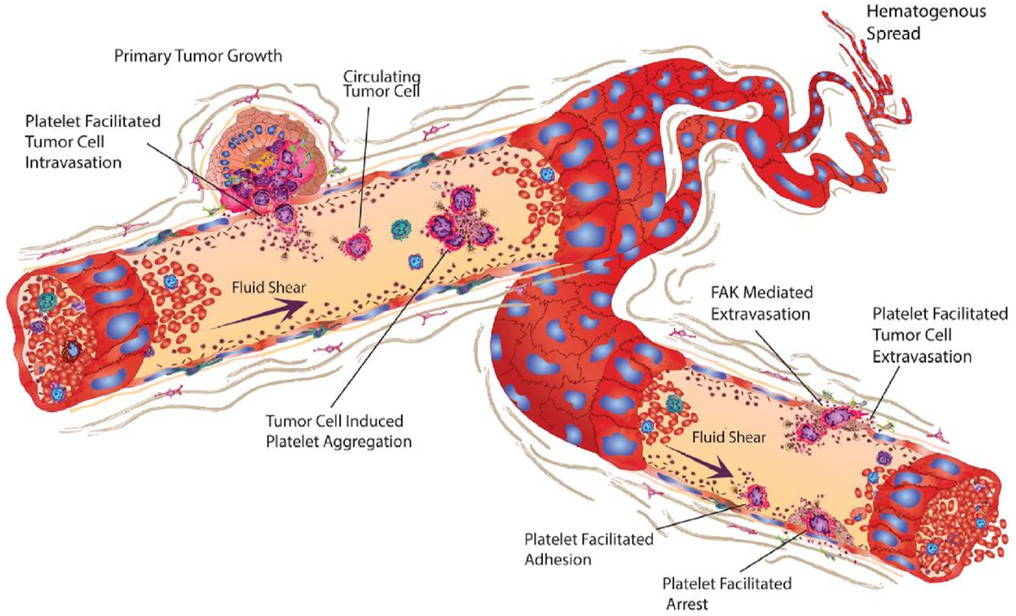
Small, in situ



Malignant

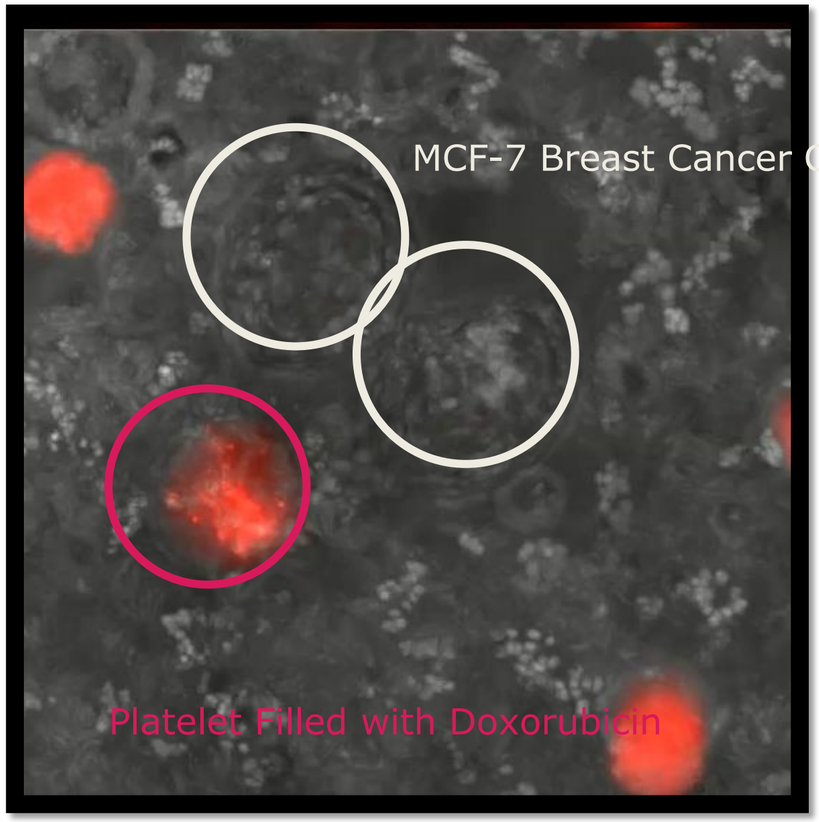
Aggressive, Metastatic

Platelets enable metastasis



Hammerle et al, Cancer Cell, 2018

Cancer Cells CONSUME Platelets



Wu et. al, Journal of Biomedical Science, 2020

Castanheira et al, Journal of Thrombosis and Haemostasis, 2021

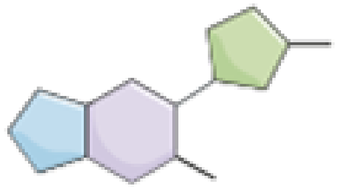
Plasfer's Patented Platelet Transfer Technology (PTT™)

Turn Cancer's *Ally* Into its *Enemy to treat the worst cancers*

Any Class of Therapeutic

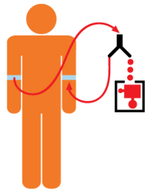
Nucleic acids

Small molecules



Proteins and peptides

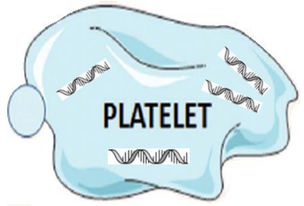
Any Platelet Source



Autologous
(patient)

Allogenic
(donor)

Loaded Platelets

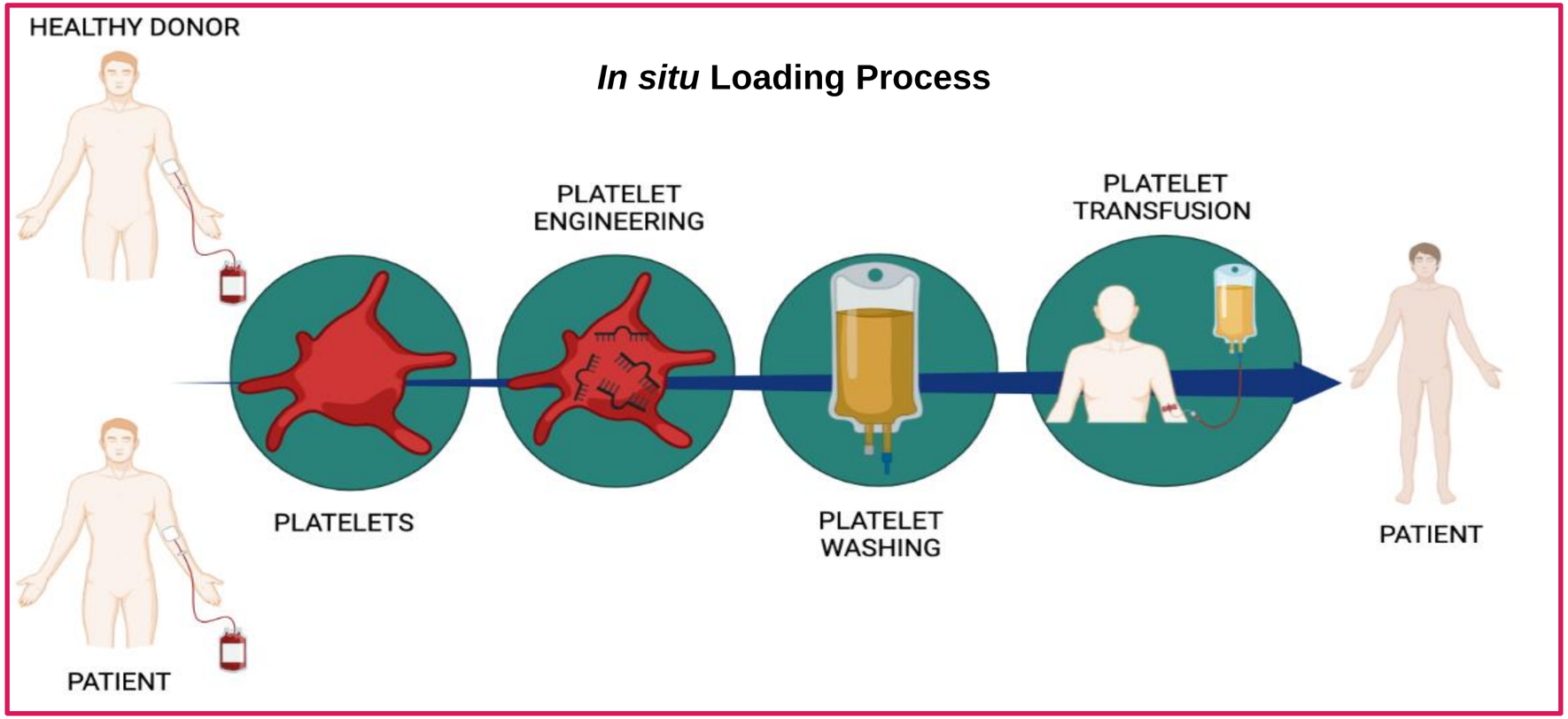


PTT™ - HOW
PTT™ Generation 1 – Product and a Process

Composition of Buffers specifically formulated to –

- Prevent platelet activation during processing
- Allow for loading of therapeutic compounds into platelets

Clear loading process, executable in a hospital treatment center by trained medical professionals



Tumor Tissue Hit List

High Clinical Need in Cancers with strong evidence of platelet/tumor interaction
An additional >1.5M patients in EU + NA per year

Type	# of EU + NA patients (Estimated 2022)	Deaths (Estimated 2022)	5 Year Survival[3] (2012-2018)	Survival with Thrombocytosis
Pancreatic Cancer	202,759	185,411	11.5%	w/ – 4.9 months w/o – 46.5 months
Glioblastoma[2]	94,960	74,370	32.5%	w/ - 4 months w/o – 11 months
Ovarian Cancer	93,323	60,504	49.7%	w/ - 2.62 years w/o – 4.65
Lung Cancer	731,071	544,817	22.9%	w/ – 38 months w/o – 63.1 months
Colorectal Cancer	700,395	308,811	65.1%	w/ – 13.3% w/o – 56.3%
Esophageal Cancer	73,799	63,991	20.6%	Worse Prognosis w/ Thrombocytosis
Gastric Cancer	165,810	110,388	33.3%	1 year w/– 72.9% 1 year w/o - 85.7% 3 year w/ – 23.4% 3 year w/o - 52.4%
Breast Cancer	812,677	190,172	90.6%	w/ - 12.5 months w/o – 26 months

Source – Global Cancer data – gco.iarc.fr Accessed April 2023

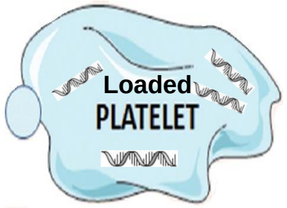
[1] Patient death used to account for patients who will likely benefit. Advanced cancers, most correlated with death, are most likely to benefit from Platelet Based Therapeutics
[2] GlobalCAN report does not separate glioblastoma from other Brain and Nervous System Cancers
[3] 5 year survival according to SEER
Note – IL6 expression increases levels of TPO, which upregulates the expression of platelets from HSPC. IL6 is a broad cytokine and modulates many other features of the immune system

Our Internal Pipeline

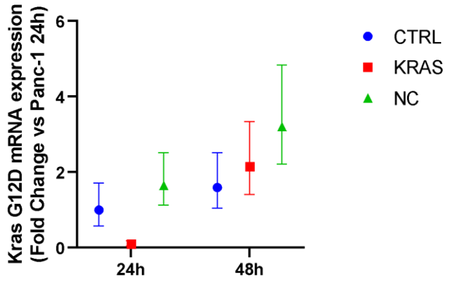
PRODUCTS	Therapeutic Area	Target/Payload	Discovery	Preclinical	Clinical
PLA-ONCO-001	Pancreatic Cancer or other locally advanced or metastatic carcinomas	Pan-KRAS			
PLA-CHEMO-001	Pancreatic Cancer or other locally advanced or metastatic carcinomas	Gemcitabine			
PLA-ONCO-002	Advanced solid cancer	Not disclosed			

PLA-ONCO-1 Preclinical Validation

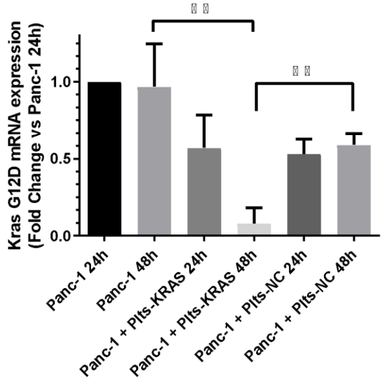
- **Lead Product Development:** PTT™-KRAS g12d siRNA platelets formulation



PTT™ + KRAS g12d siRNA
LEAD ASSET FORMULATION



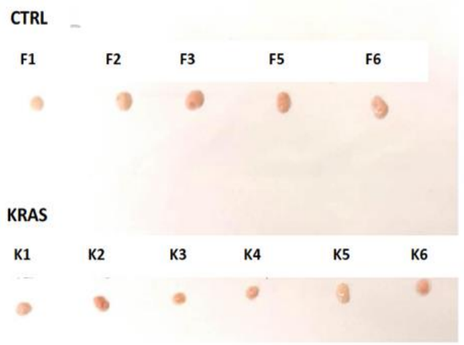
1. siRNA against the G12D mutation of KRAS transfected into Panc-1 cell line it's able to silence the mutated mRNA.

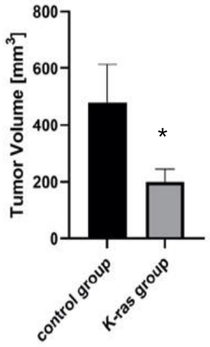


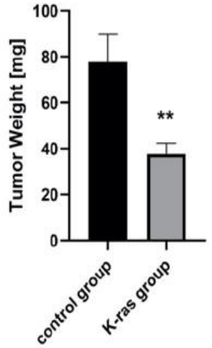
2. PTT platelets with siRNA and co-incubated with Panc-1 induced a significant reduction of G12D KRAS mRNA.

- **In-Vivo Efficacy:** PTT™-KRAS g12d siRNA platelets reduced tumor burden when compared to mock platelets by significantly and safely decreasing tumor volume and mass

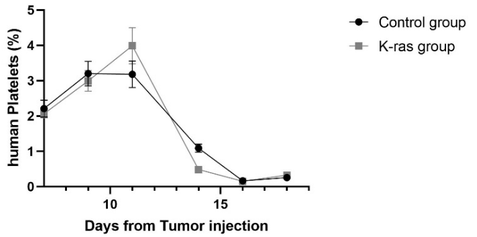
A B C





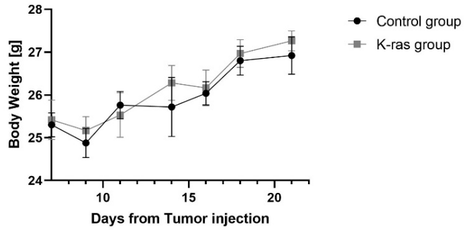


1. In a in vivo model, repeated transfusions of PLA-ONCO-1 significantly reduce tumor weight and tumor volume.



2. Same percentage of human platelet in total platelet population during treatment. n=6 mice per group.

PLATHERAPEUTICS EFFICENTLY CIRCULATE IN THE HOST
IN VIVO



3. No change in the percentage of mouse body weights, during treatment (end point). n=6 mice per group.

TREATMENT IS SAFE = NO ADVERSE EVENTS

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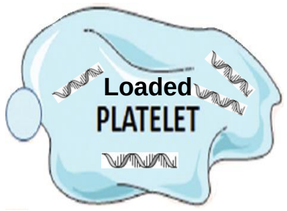
Technology and Lead Asset IP Position Consolidation



PTT™ + KRAS g12d siRNA

2022 - Lead Product Patent Application

Positive International Search Report obtained by PCT Application

- **IP-Protection-PLA-ONCO-001:** PTT™ Technology Platform and PTT™ + KRAS g12d siRNA “Lead Product” are covered

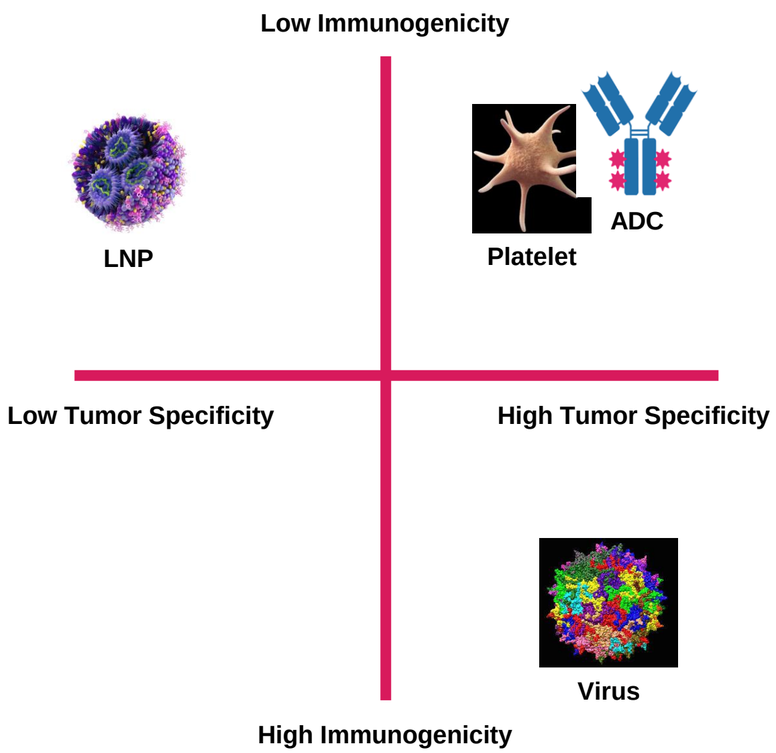
Technology	Brief Description	Patent Status
PTT™ – Platelets Transfer Technology	Platelets transfected by exogenous genetic material and platelet microparticles obtained by said transfected platelets, a method for the preparation and uses thereof for therapeutic applications.	EU Patent n. EP 2 951 292 B1
PTT ™– Platelets Transfer Technology	Platelets transfected by exogenous genetic material and platelet microparticles obtained by said transfected platelets, a method for the preparation and uses thereof for therapeutic applications.	US Patent Application n. 14/764,561
PLATHERAPEUTICS – Functionalized Platelets. Platelets transfected with siRNA and their therapeutic uses	It describes a therapeutic composition comprising blood platelets transfected with siRNA directed against a mutant form of the KRAS oncoprotein, and its use for the treatment of cancer	PCT EP2022/072484

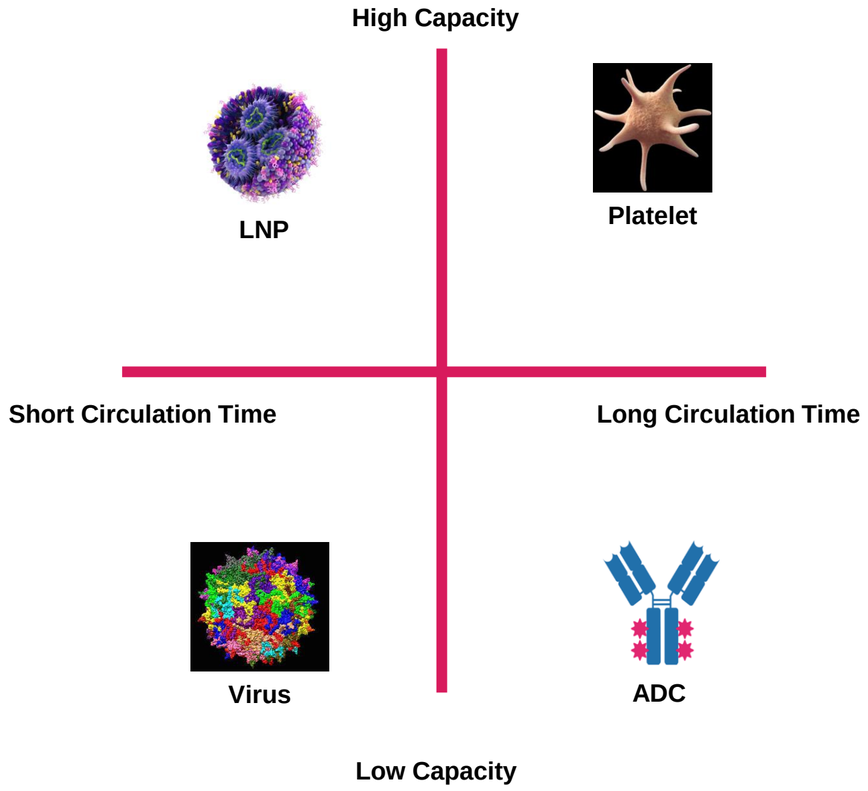
Competitive Analysis – Alternative Platforms for Drug Delivery

Targeted Drug Delivery is a Holy Grail of Drug Development

Drug Delivery

- Decades have been spent trying to optimize drug delivery
- Targeted drug delivery will:
  - Decrease side effects
  - Minimize doses needed to achieve efficacy
  - Improve patient outcomes
- Current efforts are limited by immunogenicity/low half life and/or lack of specificity
- Platelets are superior to other vehicles due to their long circulation time, high loading capacity, low immunogenicity and high specificity to tumor cells





Team

Strong Team of Platelet Experts, Experienced Drug Developers and Entrepreneurs

Paolo Gresele – Founder and CSO

- Internationally recognized expert of platelet biology and physiology
- Co-Inventor of PTT platform

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Marco Malvestiti – Founder and CEO

- Serial entrepreneur
- Co-Inventor of PTT platform

Unlocking the Power of Platelets

Rosario Billetta – COO

- Biotechnology manager and consultant

Luigi De Marco – CMO

- Cryopreservation and Transfusion Expert

Chris Bethel – CIO

- Pharma/Drug development
- Innovation Management

Company Development Plan

Founders' → **Seed Round** → **Round Q4-2020** → **Pre-series A** → **Expected Q1-2024** → **Series A**

PRODUCTS	Therapeutic Area	Target/Payload	Discovery	Preclinical	Clinical
PLA-ONCO-001	Oncology	siRNA - KRAS g12d	In Vivo Efficacy		

PTT™ DEVELOPMENT

Milestones:
- Proof of Concept – Platelet mediated drug delivery
- Develop 1st asset to Preclinical-Phase
- IP Expansion

2021

PRODUCTS	Therapeutic Area	Target/Payload	Discovery	Preclinical	Clinical
PLA-ONCO-001	Oncology	siRNA - KRAS g12d		IND Enabling	
PLA-CHEMO-001	Oncology	Chemotherapeutic - Gemcitabine		IND Enabling	
PLA-ONCO-002	Oncology	Target Not Disclosed		POC	

Milestones:
- Develop 1st asset to Pre-IND
- Develop PLA-ONCO and PLA-CHEMO program
- Partnering (Co-development) with large pharma

2024

PRODUCTS	Therapeutic Area	Target/Payload	Discovery	Preclinical	Clinical
PLA-ONCO-001	Oncology	siRNA - KRAS g12d			IND Ready - Ready to enter Phase 1
PLA-CHEMO-001	Oncology	Chemotherapeutic - Gemcitabine			IND Ready - Ready to enter Phase 1
PLA-ONCO-002	Oncology	Target Not Disclosed		Pre-IND	

Milestones:
- Develop 1st and 2nd asset to Phase I
- Develop 3rd asset to Pre-IND
- Establish Plasfer as leading Platelet-based cell-therapy company asset to Pre-IND

2026

2029

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Unlock The Power of Platelets

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