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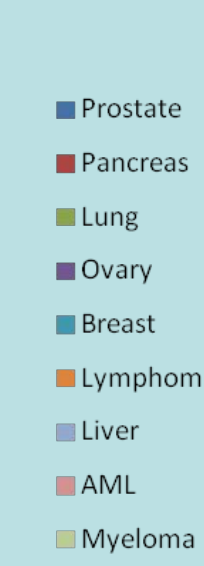
## What about IMODI

The national IMODI (Innovative MODEls initiative) consortium including 25 partners (pharmas, SMEs, academic research labs and clinical centers) aims at developing more predictive tools for better selection of new effective treatments to combat 9 cancer pathologies. These developments include:

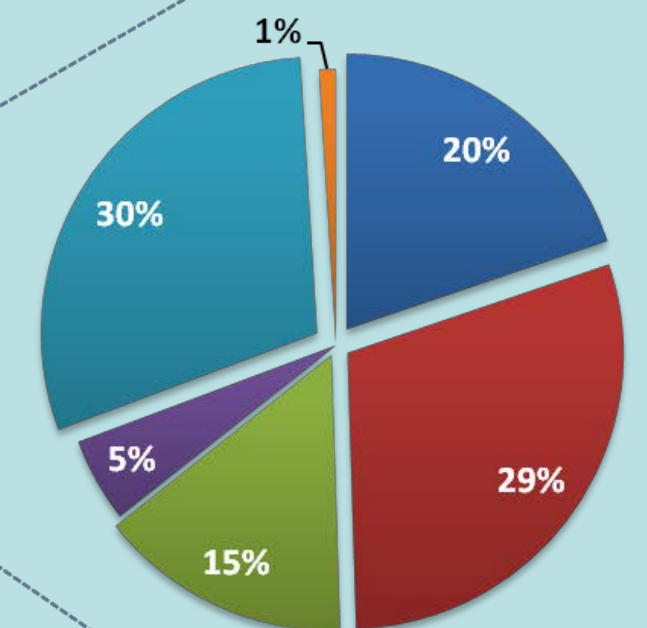
- Collection of *in-vivo* PDX models,
- Collection of *in-vitro* derived cell lines,
- 2D & 3D ex-vivo assays,
- In-vivo* humanized models (immune system, liver and tumor stroma),
- Characterization of tumor histology, gene mutation, gene expression, pharmacological responses, gut microbiota,
- Biobanks of tumors, blood, serum and stools,
- Central data base,
- Data mining,

Results on NSCLC lung cancer model developments, characterization and data analysis are presented as an example of the IMODI holistic and integrative approach.

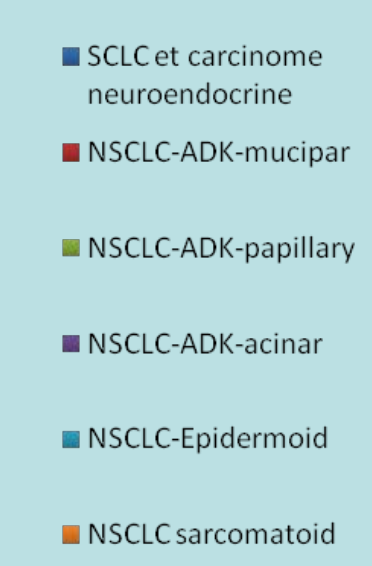
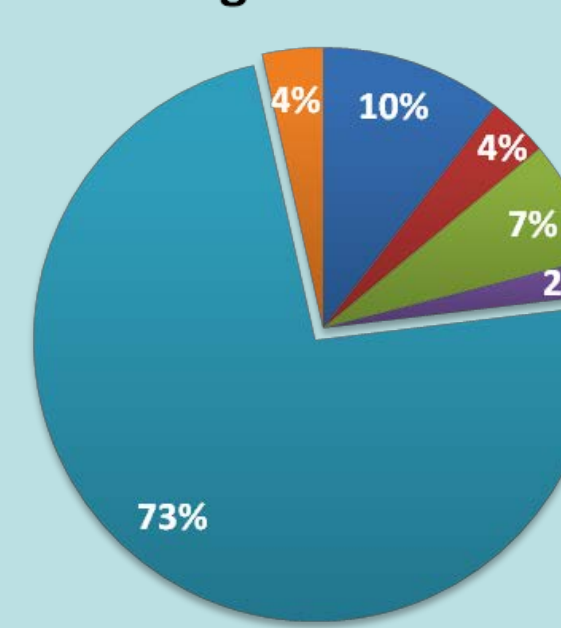
### Nb PDX collection under development



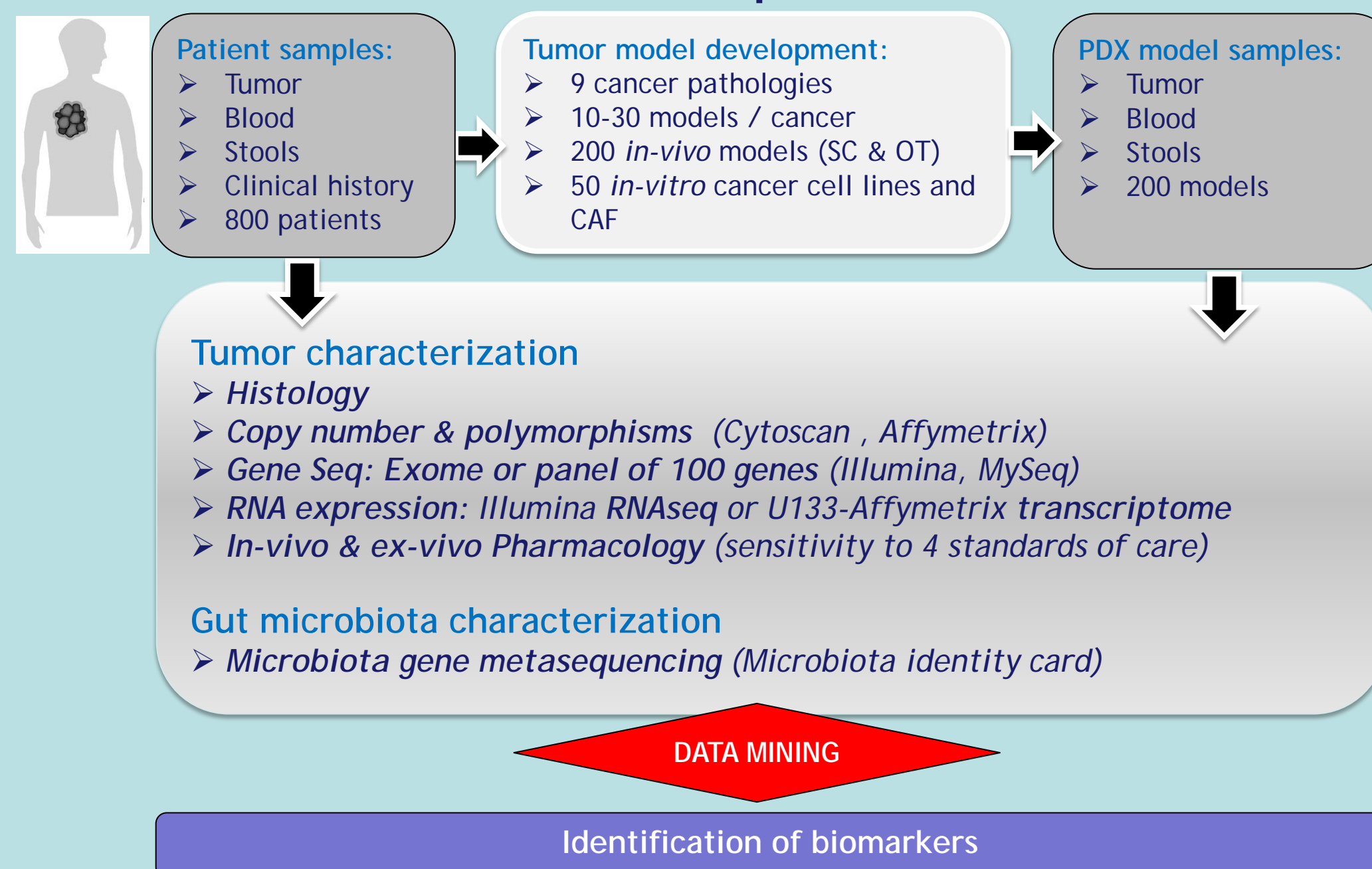
### % Lung cancer Patients population



### % Lung PDX models



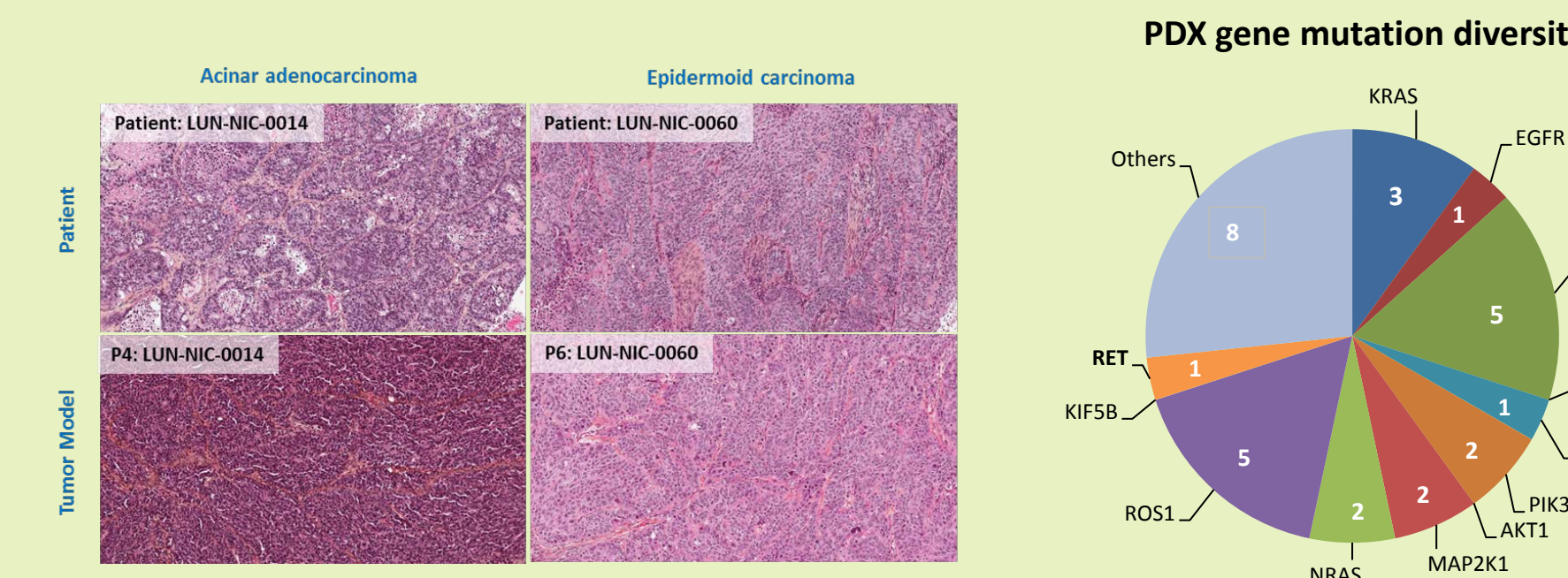
## General process



## Histology and Genomic Characterization

Example of a well characterized NSCLC PDX collection

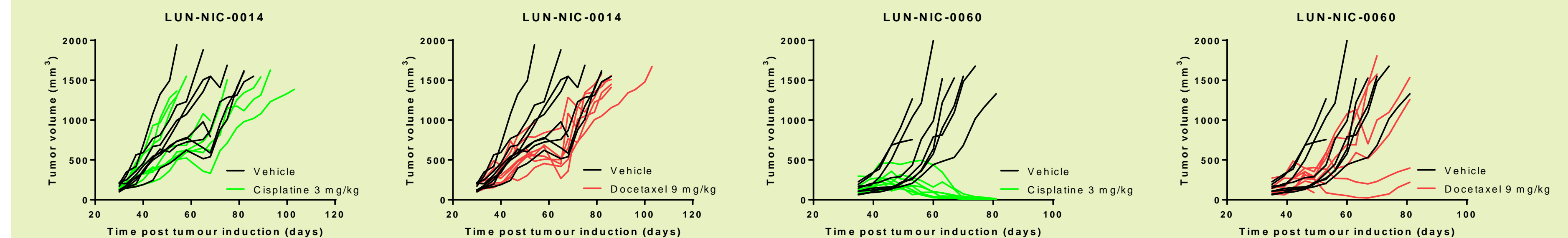
- Highly conserved phenotype and genotype
- Histological PDX profile are in concordance with those observed in the patient's tumor
- Major molecular subtypes are represented in the NSCLC collection
- EGFR-mutated models are under development



## In-vivo Pharmacological Response to Standards of Care

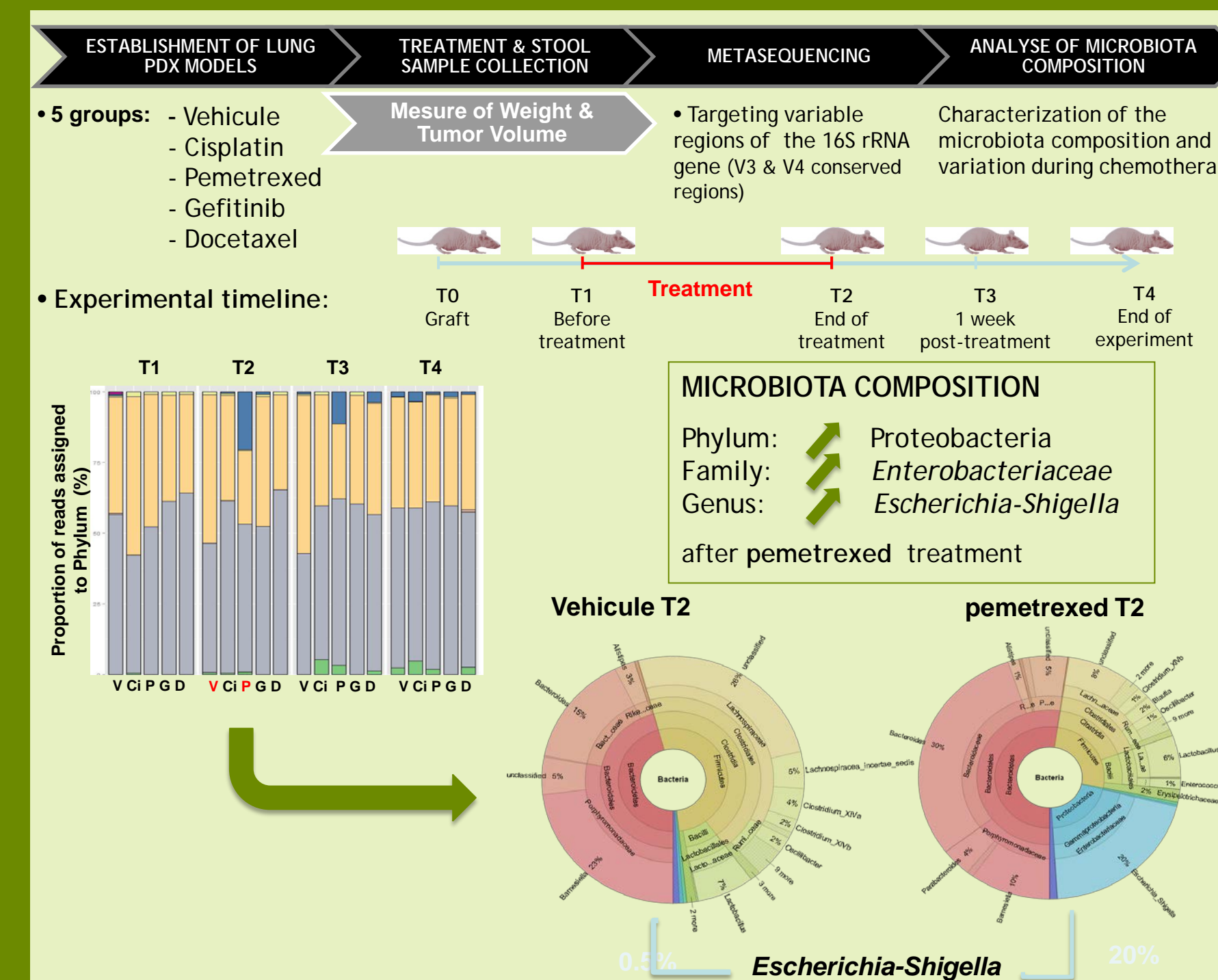
- Significant efficacy of cisplatin and gemcitabine on the LUN-NIC-0060 epidermoid model
- Marginal activity of gefitinib on the LUN-NIC-0014 acinar adenocarcinoma model (EGFR wt, KRAS wt, BRAF wt, ALK wt, ROS1 wt)
- LUN-NIC-0014 PDX response to cisplatin and docetaxel correlates with patient outcome (non responsive to cisplatin + docetaxel)

Drug	ΔT/ΔC (%) (LUN-NIC-0014)	ΔT/ΔC (%) (LUN-NIC-0060)
Cisplatin 3 mg/kg	64	-4
Pemetrexed 75 mg/kg	51	Non-tested
Gefitinib 100 mg/kg	37	Non-tested
Docetaxel 9 mg/kg	59	75
Gemcitabine 120 mg/kg	Non-tested	-10

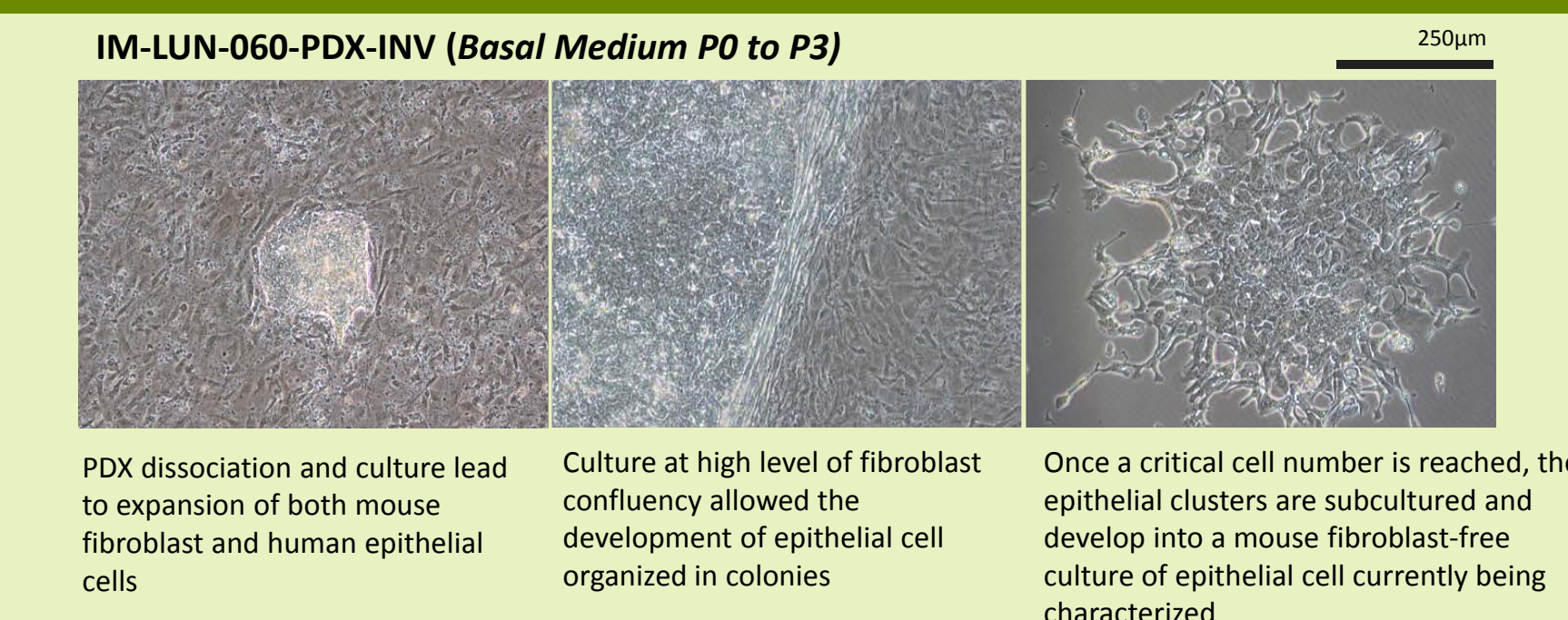


RESULTS

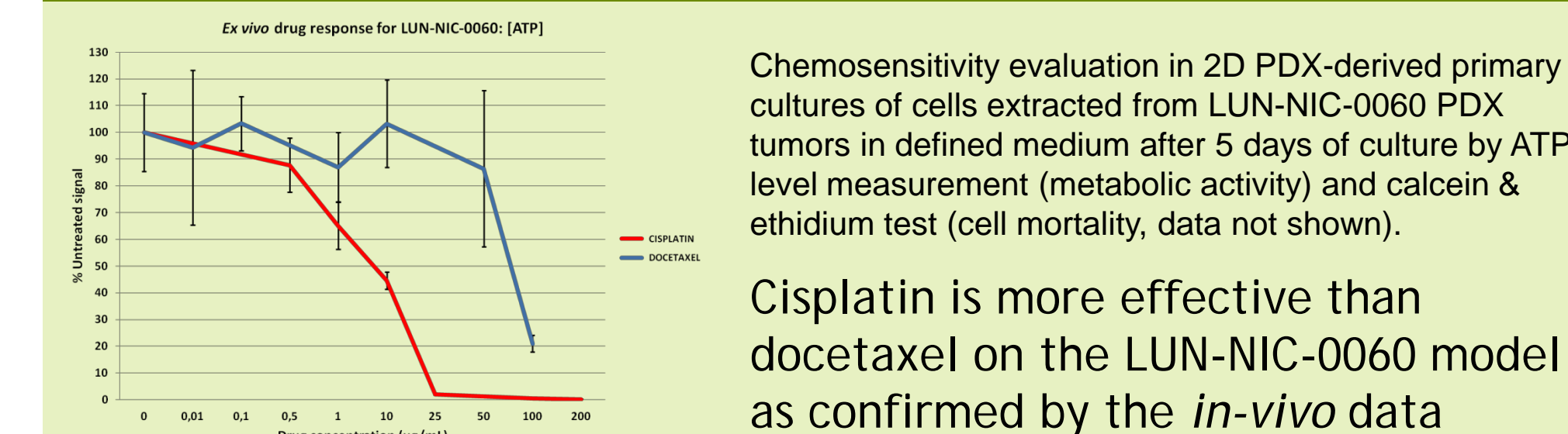
## Gut Microbiota Analyses



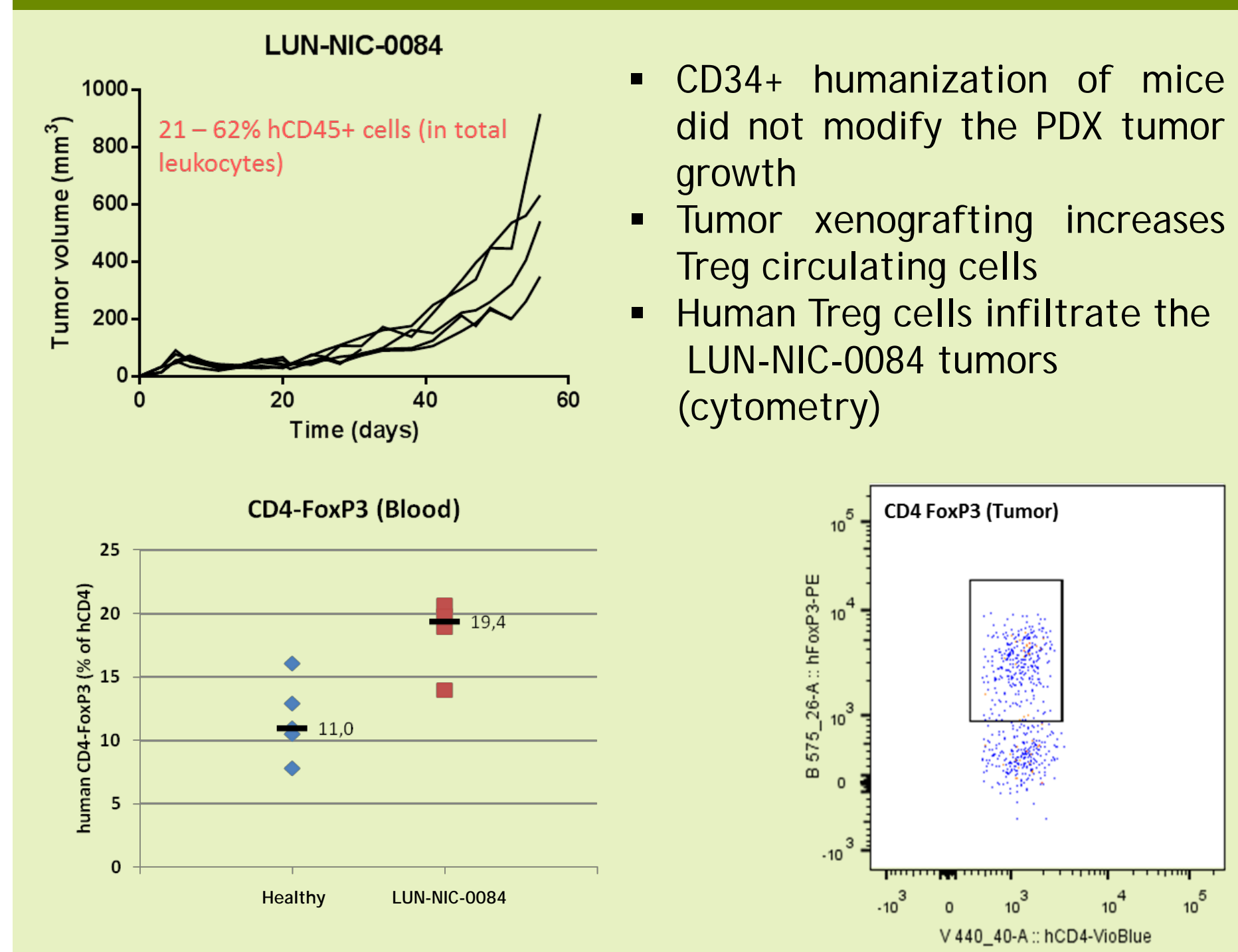
## In-vitro PDX-Derived Cell Line Establishment



## Ex-vivo Pharmacology Assay



## Tumor Microenvironment Humanization



## Conclusion and perspectives

- IMODI is an operational consortium to continuously deliver new predictive models in regards to specific clinical needs and diversity,
- All results are available for new therapeutic and diagnostic candidate selection,
- Ex-vivo* assay predicts *in-vivo* cisplatin and docetaxel sensitivity in a lung PDX model (other drugs and models are under investigation),
- Chemotherapeutic agents could impact the microbiota composition and microbiome analysis could learn about drug toxicity and tumor response,
- 2<sup>nd</sup> generation of PDX model with human microenvironment would help the selection of clinical drug candidates (impact of the humanization on the pharmacological drug profile is pending).