

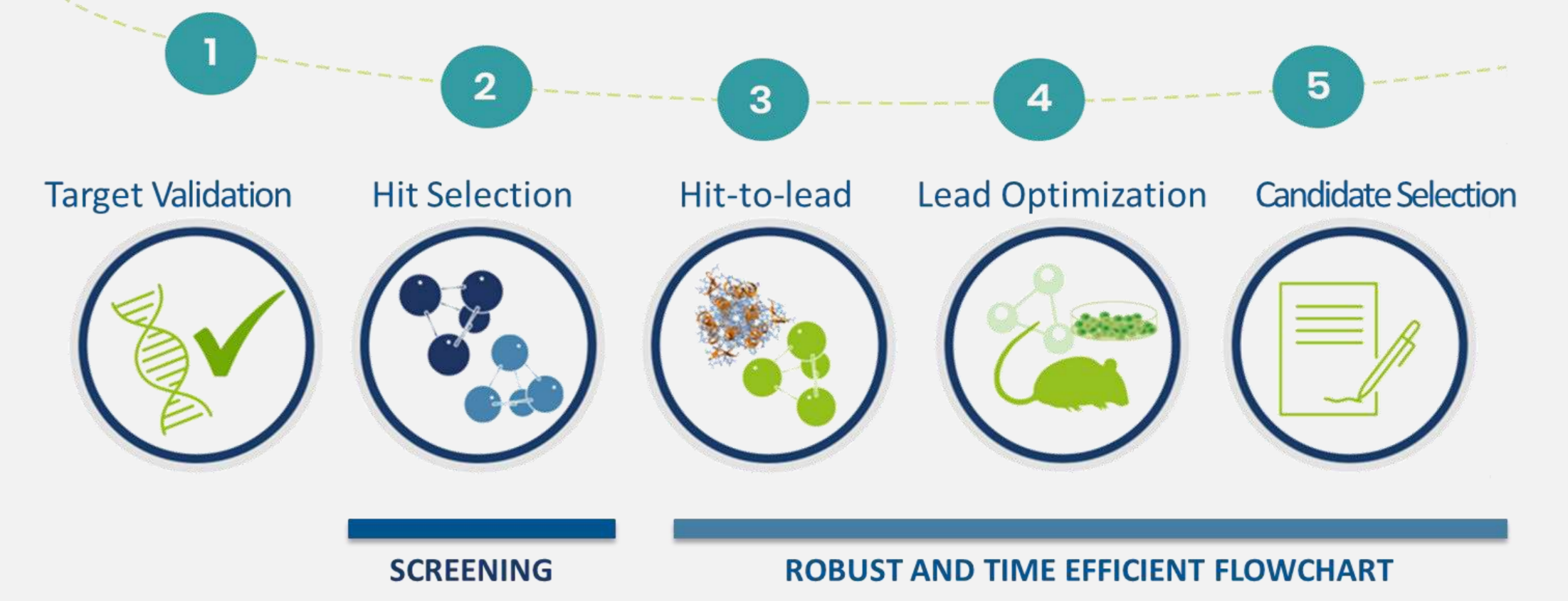
Development of Pre-Clinical Assays to Support Drug Discovery Programs in Immuno-Oncology

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1 CONTEXT & OBJECTIVES

The use of immunotherapies in oncology has drastically changed the way of treating cancer, providing innovative and efficient therapeutic solutions to patients in medical needs. As a consequence, tremendous R&D efforts are done in immune-oncology to discover new targets and develop new drugs. In that context, the use of relevant and robust assays to predict therapeutic efficiencies has become a key for drug discovery programs.

At OncoDesign, we have gathered our experience and scientific expertise in immune-oncology to develop and provide solutions to support your drug discovery projects in immune-oncology, from hit identification to candidate selection, on a stand alone basis or through integrated drug discovery solutions.



2 RESULTS – in vitro/ex vivo Assays

✓ HIGH THROUGHPUT PLATFORM FOR ICD SCREENING

Some chemotherapeutics induce a type of cell stress and death that is immunogenic, converting the patient's dying cancer cells into a vaccine that stimulates antitumor immune responses.

Read-out: DAMPs (CRT, HMGB1 and ATP) released during ICD recruit and activate immune cells (DC, monocytes, T cells)

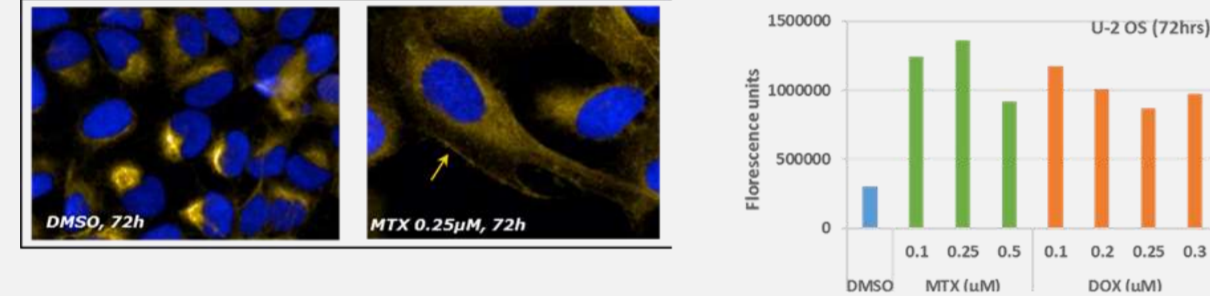
Increase of extracellular ATP content (ENLITEN® Promega) at non-toxic doses determined by CellTiter-Glo® (Promega)

	U-2 OS		MDA-MB-231		HEPA 1-6	
	Viability	ext ATP	Viability	ext ATP	Viability	ext ATP
MTX 0.2 µM	84%	757%	84%	786%	92%	237%
Doxo 0.2 µM	90%	647%	94%	297%	95%	254%

Increase of HMGB1 secretion at non toxic concentration

	U-2 OS		MDA-MB-231		HEPA 1-6	
	Viability	ext ATP	Viability	ext ATP	Viability	ext ATP
MTX 0.2 µM	84%	757%	84%	786%	92%	237%
Doxo 0.2 µM	90%	647%	94%	297%	95%	254%

Increase of extracellular plasma membrane calreticulin amount in the absence of cell toxicity

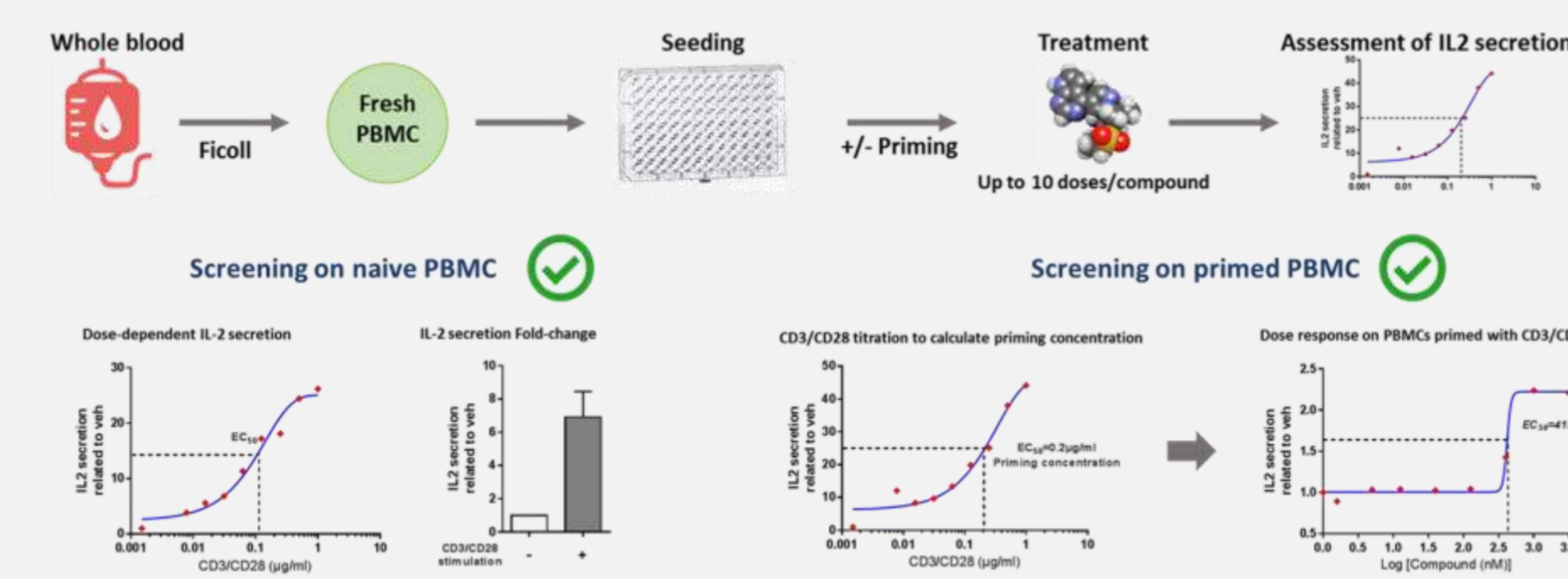


→ Set for 10-20K screening campaigns

✓ PHENOTYPIC ASSAYS TO SUPPORT YOUR DRUG DISCOVERY FLOWCHART

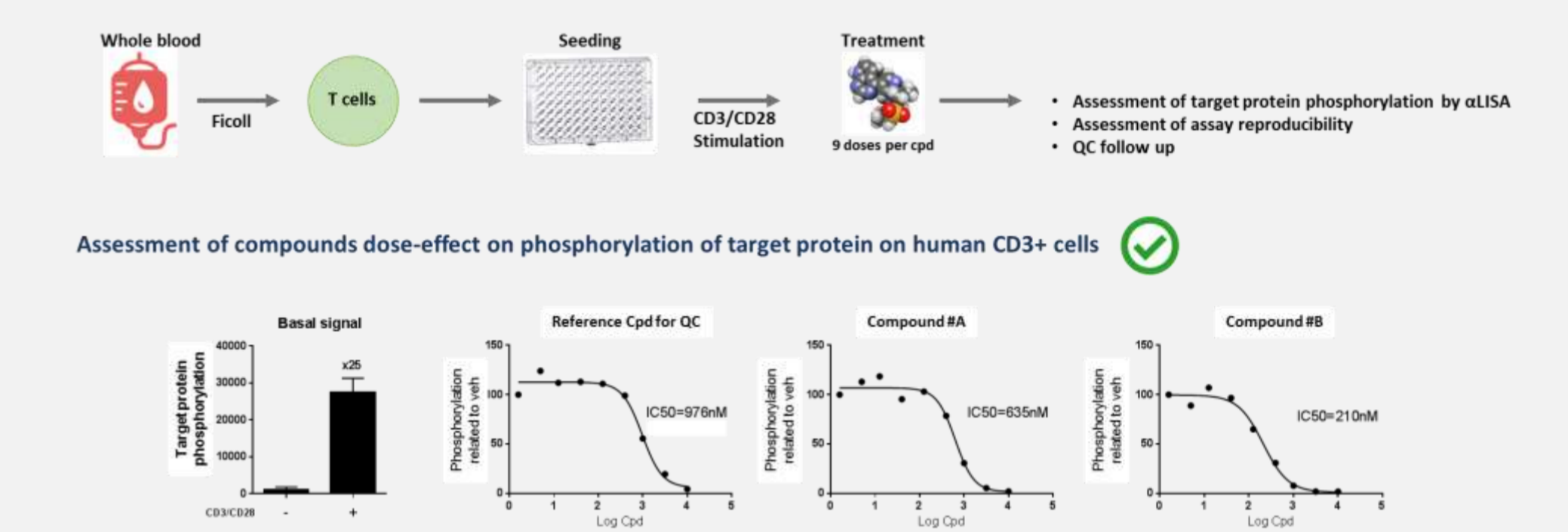
	Naive/Primed PBMC	T cells	T cells	Splenocytes	moDCs	Macrophages
Species	Human	Human	Human	Murine	Human/Mice	Human
Starting Material	Whole blood	Whole blood	Whole blood (T cells) & Raji cell line	Spleen	Whole blood → Monocytes	Whole blood → Monocytes
Type of Assay	Cytokine secretion	Cytokine secretion	CTL	Cytokine secretion	Differentiation	Differentiation
Read-out	IL2	IFNγ	Raji lysis	IFNγ	DCs phenotype	M2 phenotype
Technology	AlphaLISA	ELISPOT	Flow cytometry Luminescence	ELISPOT	Flow cytometry	Flow cytometry
Throughput	Medium	Medium	Medium	Medium	Low	Low

➤ PBMC activation phenotypic assay



✓ A LA CARTE ASSAYS INTEGRATED IN DRUG DISCOVERY FLOWCHARTS

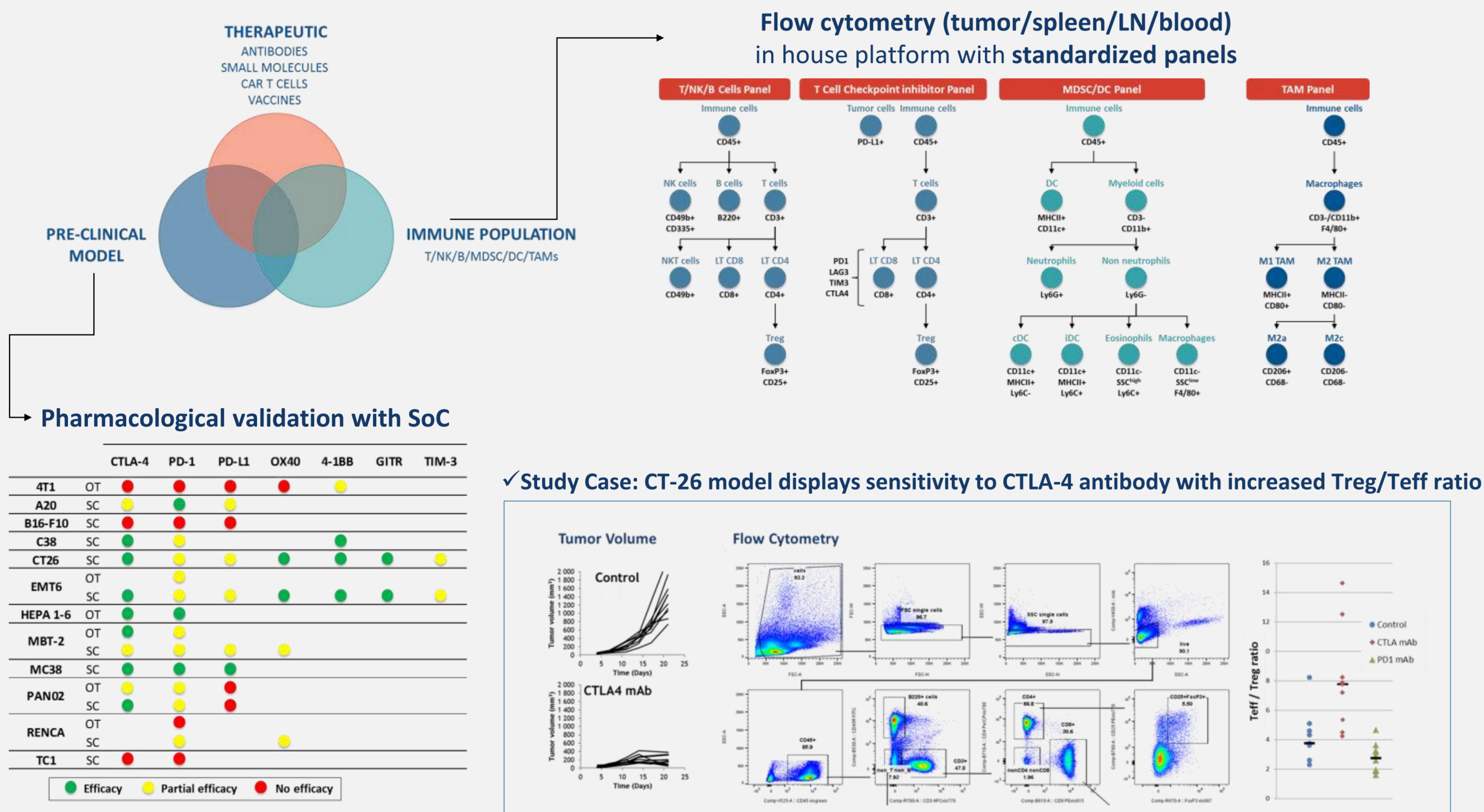
✓ Study Case: Assay developed to support lead optimization phase – weekly basis



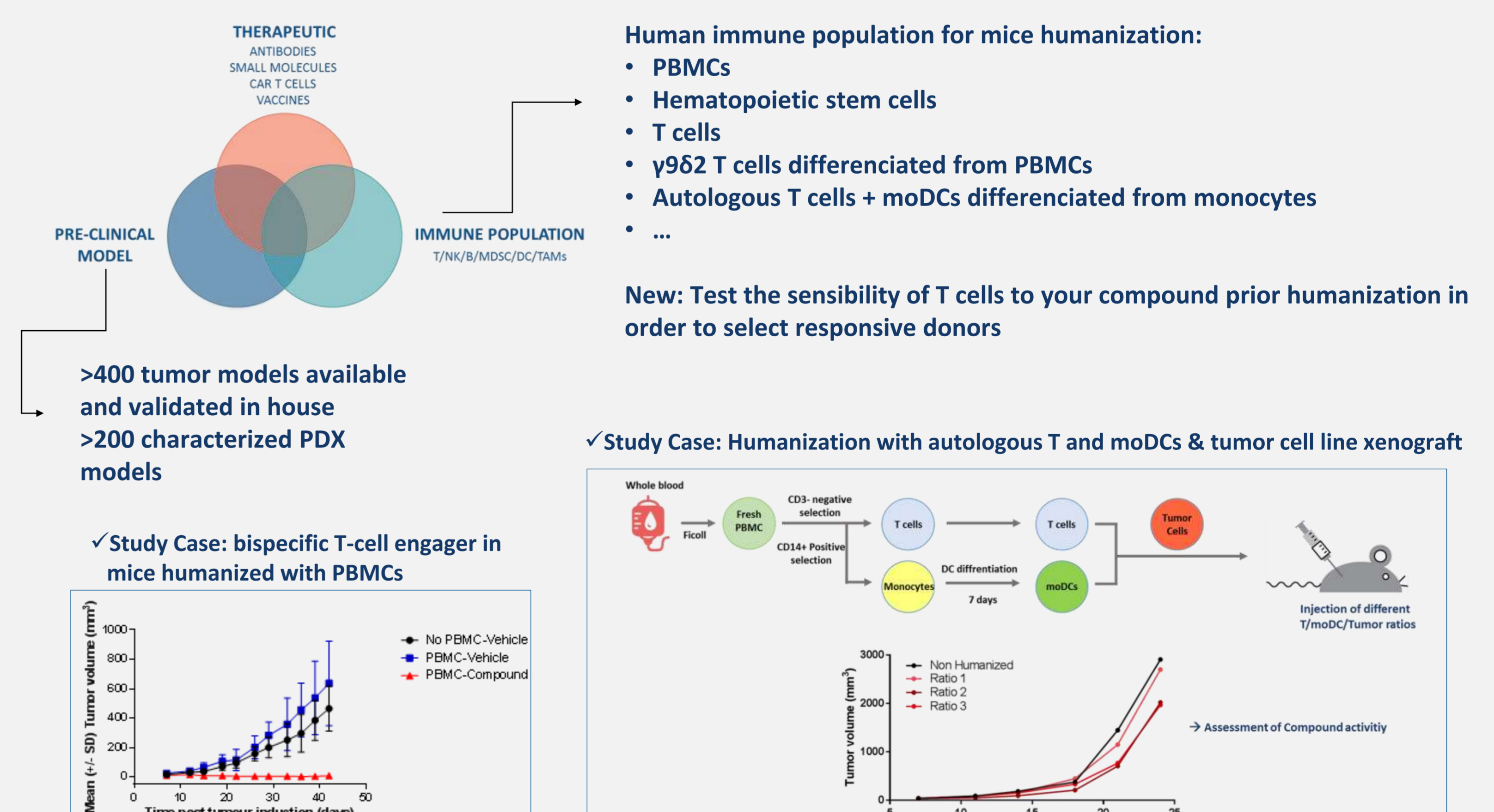
- ✓ Easy access to whole blood & test on multiple donors
- ✓ Various and adaptable read-outs
- ✓ Experience in cell culture and phenotyping
- ✓ Experience in developing cell-based assays with small molecules and biologics

2 RESULTS – in vivo Syngeneic/Humanized Assays

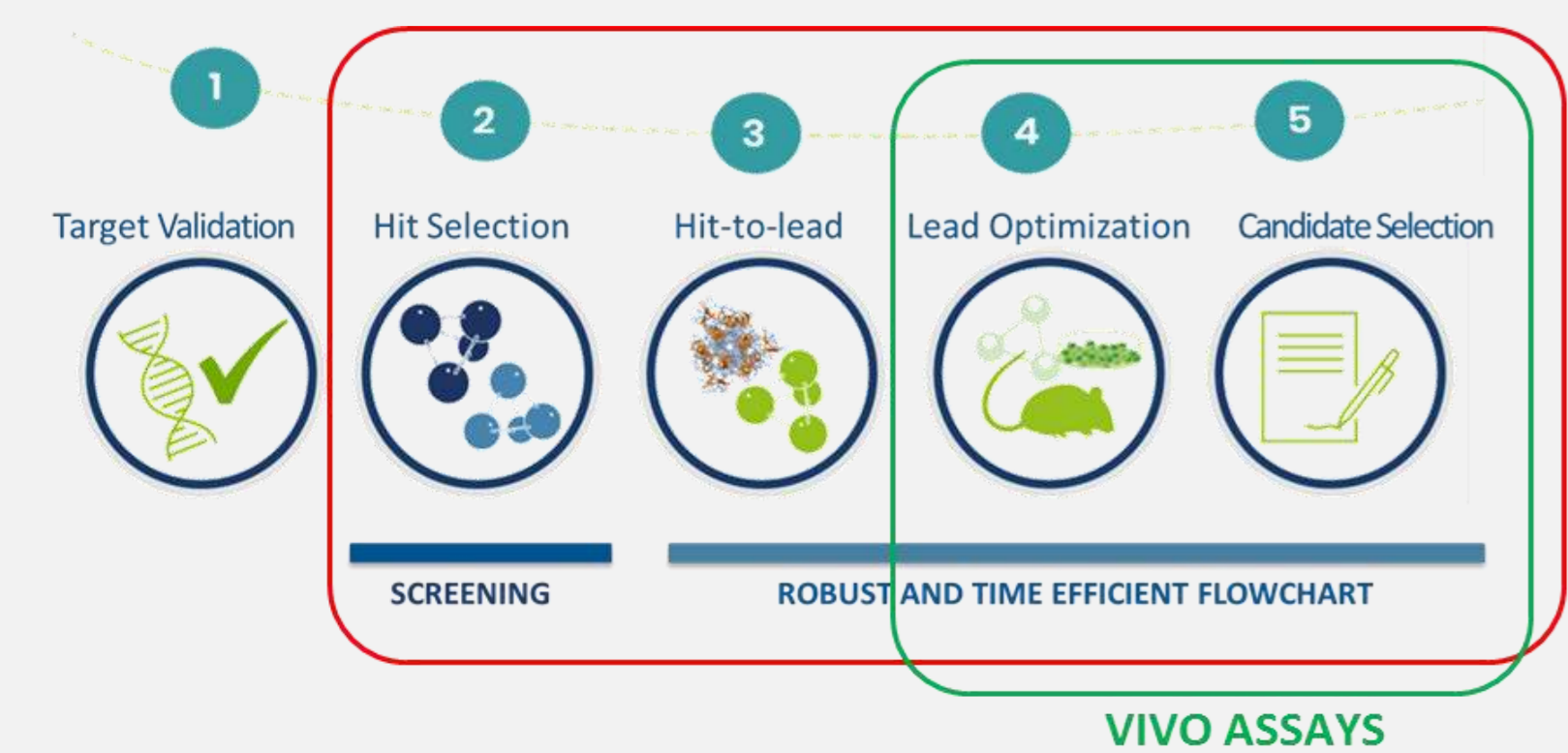
✓ SYNGENEIC MODELS: 500+ PRECLINICAL PROJECTS PERFORMED



✓ HUMANIZED MODELS: 150+ PRECLINICAL PROJECTS PERFORMED



3 CONCLUSION



- ✓ ONCODESIGN HAS DEVELOPED VITRO/VIVO MODELS TO COVER YOUR DRUG DISCOVERY PROJECT AT ALL STAGES
- ✓ YOU CAN INTEGRATE OUR ASSAYS INTO YOUR FLOWCHART
- ✓ OUR NEW FACILITIES AND CORE EXPERTISES IN MEDICINAL CHEMISTRY, DMPK AND BIOANALYSIS, ONCODESIGN ALSO OFFERS FULLY INTEGRATED DRUG DISCOVERY SERVICES.