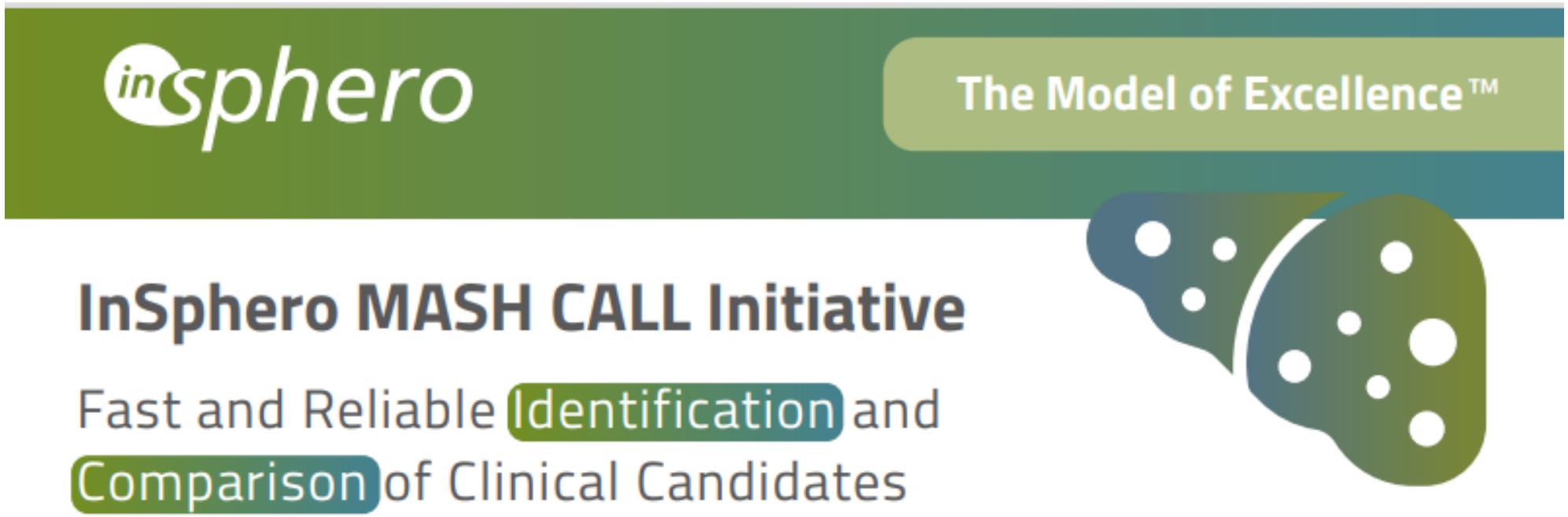
Identification of drug candidates in MASH fast and cost-effectively with MASH CALL

Join the MASH CALL Initiative

Deadline September 6th



Why engaging in a MASH CALL?

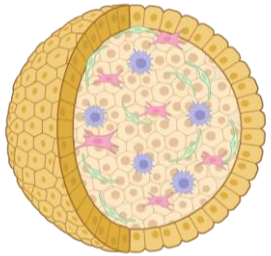
- Fast and translational MASH phenotypic candidate selection process
- Cost-effective human pre-clinical model
- On demand combinatorial drug approach
- Possibility to a comprehensive phenotypic analysis follow-up
- Benchmarking with clinical candidates

PATH TO A SUCCESFUL MASH CLINICAL CANDIDATE

How do you benefit? MASH CALL content

MASH CALL – 40 days since start until report delivery

Drug testing in Human Liver Microtissue 3D InSight™ MASH model



- **6-concentration dose-response**
- **3 replicates**

ENDPOINTS FROM SAME ASSAY

Toxicity	Extracellular LDH Time course
Steatosis	Triglycerides
Fibrosis	Secreted Pro-Collagen 1 (2 time points)

CLINICAL AND TRANSLATIONAL BENCHMARKING

- Comparison against up to 20 clinical candidates
- Comparison against reference controls and healthy model

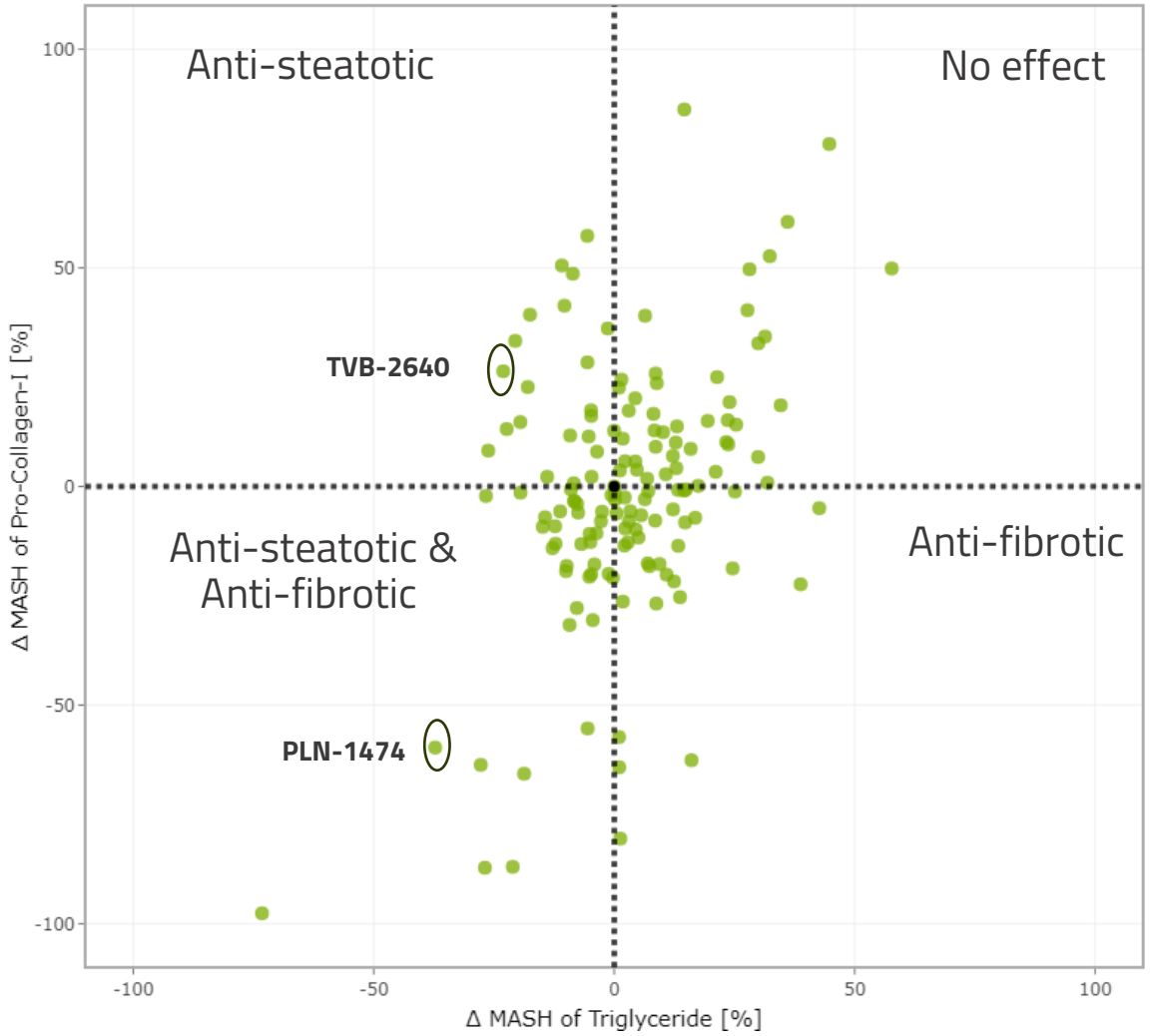
Anti-steatotic and anti-fibrotic comparison of 20 clinical candidates

Set up call for a deeper dive into the data!

Examples of effects of clinical candidates matching MOA:

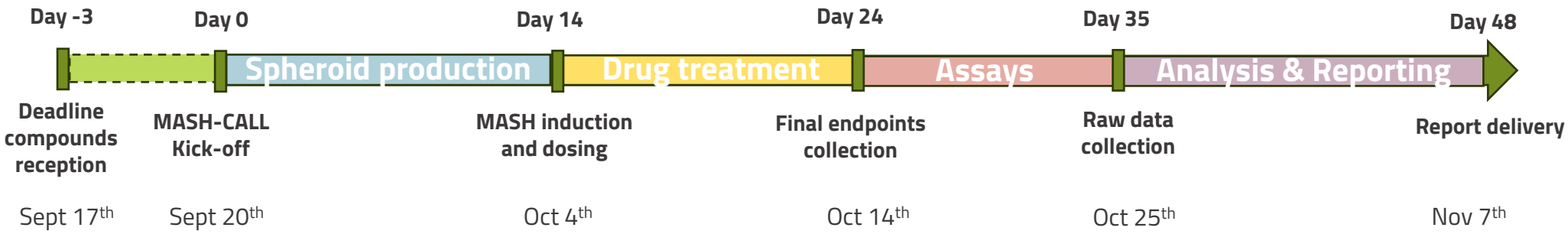
TVB-2640, a fatty-acid synthase enzyme inhibitor, has **anti-steatotic** effects

PLN-1474, a small-molecule selective inhibitor of the integrin αvβ1, shows both **anti-steatotic and anti-fibrotic effects**



*Each clinical candidate measured in 3 concentrations (1 dot/concentration)

Timelines MASH CALL



Phase 1 MASH CALL and Phase 2 follow-up

Phase 1

MASH CALL

Drug candidate screening and selection

With a 6-concentration dose-response range in 3 replicates

ENDPOINTS

- LDH
- Triglycerides
- Pro-Col1

Phase 2: Validation study and extended phenotypic analysis

- **Increased sample size (n=6)**
- **Optimized concentrations (selected from phase 1)**
- **Validation of results**
- **Additional confirmation with comprehensive phenotypic analysis**
- **Flexibility of selection of endpoints (modularity) and time of execution**

Pathophysiological Hallmarks	Offered Modular Assays
Steatosis	Total intracellular triglycerides
	Bodipy staining
Inflammation	Cytokine multiplex 6 markers (TNF-α, IL-6, IL-8, MCP-1, MIP-1α, IP-10)
Fibrosis	Pro-collagen I (ELISA) – 2 time points
	Pro-collagen III (ELISA) – 2 time points
	MMP1, MMP2, MMP3, MMP9, TIMP1 (Luminex)
	Histology Sirius Red Staining
Samples collection	Collection of media supernatants for follow-up assays
	Pre-collection of samples for fibrosis quantification (Fibronest, Pharmanest)
	Pre-collection of samples for transcriptomics
Additional modules	Fibrosis quantification digital pathology (Fibronest, Pharmanest)
	Transcriptomics (TempO-Seq, DRUG-Seq, low-input RNA-Seq)

THANK YOU

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