inventiva

Jefferies

Jefferies Virtual Healthcare Conference

June 2 – June 4, 2020

Developing breakthrough therapies in NASH and MPS

Corporate Presentation

June 2020

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Inventiva: highlights

- Clinical stage biotech with focus on **oral small molecules for high unmet need** in fibrosis, lysosomal storage disorders and oncology

- **Two unencumbered late stage assets** in two high value indications
  - **Lanifibranor** – only pan-PPAR agonist in clinical development for NASH, Phase IIb data due in June
  - **Odiparcil** – first orally available therapy for MPS

- **A clinical stage partnership with AbbVie**
  - **ABBV-157 RORγ program** with potential in several auto-immune indications currently in clinical development in patients with psoriasis
  - Inventiva eligible to milestone payments and sales royalties

- **Compelling early stage pipeline**
  - YAP-TEAD program in late pre-clinical stage approaching clinical candidate selection

- **State of the art R&D capabilities** including wholly owned 'pharma scale' discovery facilities with a **discovery engine** focused on nuclear receptors, transcription factors and epigenetic targets
  - 240,000 compound library, 60% of which are proprietary

- **Strong US and European shareholder base and experienced senior management** team with a track record of operational and scientific excellence

- Cash position allowing a **runway until end of Q3 2021**

Lanifibranor: the only pan-PPAR agonist in clinical development for the treatment of NASH

- **Moderate and balanced pan-PPAR agonist activity** (PPARα, PPARγ and PPARδ) with differentiated chemical structure
- **Once daily oral administration**
- **Efficacy demonstrated** on insulin-sensitivity, dyslipidemia, steatosis, ballooning, inflammation, hepatic fibrosis and cirrhosis in preclinical models
- **Phase IIa**(1) **trial demonstrated pan-PPAR agonist activity,** supporting dose selection for NASH clinical trial
- **Favorable safety profile** demonstrated in:
  - 24-months rodent and 12-month monkey studies leading to **PPAR class clinical hold lifted** by FDA
  - Phase I trials with more than **200** healthy volunteers(2) and Phase IIa study with **47** TD2M patients
  - Approximately **250** patients have been treated for 24 or 48 weeks in our ongoing and completed Phase IIb clinical trials
  - In connection with these trials, lanifibranor has undergone a total of **7 positive DSMB reviews**
- Composition of matter patent delivered in 59 countries and method of use patent granted in the US, China and in the EU: **limit of exclusivity 2035**
- **FAST Track** designation granted by FDA

(1) Conducted by Abbott prior to our funding; (2) Including 125 healthy volunteers in the phase I conducted by Abbott prior to our funding

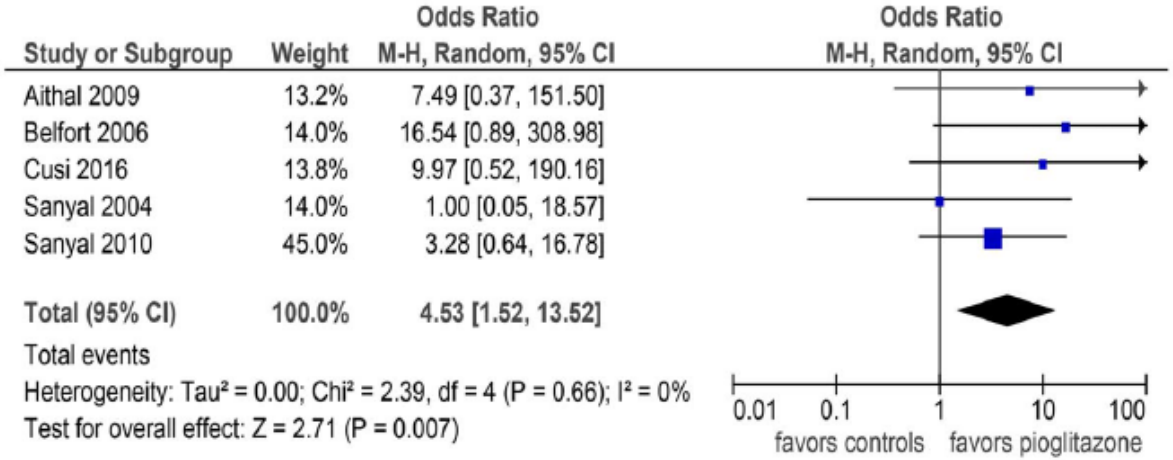
PPARγ efficacy is well established in NASH

Compound	PPARα EC50 (nM)	PPARδ EC50 (nM)	PPARγ EC50 (nM)
▶ Lanifibranor	1630	850	230
▶ Pioglitazone	-	-	263

PPARγ activation by pioglitazone improves steatosis, ballooning, inflammation and metabolic markers in NASH patients after 6 months or 18 months of treatment

Pioglitazone (PPARγ)	Belfort NASH study 6 month treatment			Cusi NASH study 18 month treatment		
	Placebo	Pio	P	Placebo	Pio	P
Steatosis (% patients improved)	38%	65%	0.001	26%	71%	< 0.001
Inflammation (% patients improved)	29%	65%	0.001	22%	49%	= 0,004
Ballooning (% patients improved)	24%	54%	0.001	24%	51%	= 0,004
NASH resolution (% patients)	-	NA	-	19%	51%	< 0.001
Fibrosis (mean change in score)	-	NS	-	0	- 0.5	= 0.039

Pioglitazone improves advanced fibrosis



- **Pioglitazone improves advanced fibrosis** (stage F3-F4) as indicated by an increase in the number of NASH patients whose fibrosis stage changed from F3-F4 to F0-F2 at the end of treatment

Source: Corey KE and Malhi H, Hepatology 2016. Note: clinical trial not conducted by Inventiva

PPARγ activity can also be reinforced by PPARδ efficacy

- Anti-inflammatory effects of lanifibranor mediated through PPARδ activation reported in preclinical models
- Seladelpar (potent selective PPARδ) phase IIb trial reported encouraging results in the 152 patients having paired biopsies at entry and end-of-study, out of the 181 patients enrolled in a 52-week biopsy trial in NASH

52-week phase IIb preliminary topline results	Placebo (N = 25)	Seladelpar 10 mg (N = 39)	Seladelpar 20 mg (N = 42)	Seladelpar 50 mg (N = 46)
Fibrosis improvement (≥1 stage) with no worsening of NASH	20.0%	23.1%	23.8%	37.0%
Resolution of NASH with no worsening of fibrosis	8.0%	10.3%	19.0%	26.1%
Fibrosis improvement and resolution of NASH	8.0%	5.1%	11.9%	19.6%

- Considering fenofibrate (PPARα) and elafibranor (dual PPARαδ with preferential α activity) NASH trials, PPARα activation alone seems insufficient to lead to NASH resolution
  - Fenofibrate open label study (48 weeks of treatment): no statistical significant results (trend in ballooning improvement)
  - Elafibranor Phase III NASH resolution (18 months of treatment): 19,2% vs 14,7%, p = 0.0659
  - Elafibranor phase II NASH resolution (12 months of treatment): 19% vs 12%, p = 0.045
    - In a sub-analysis of patients with NAS≥4 and randomized in centers that included in each treatment arm patients with decrease of at least 1 point: steatosis: 35% vs 18%, p = 0.10 / inflammation: 55% vs 33%, p < 0.05 / ballooning: 45% vs 23%, p = 0.02

Source: Lefere S, et al. J Hepato. 2020; Cymabay fourth quarter press release March 2020; Ratziu V, et al. Gastroenterology 2016. Note: (1) GOLDEN 505 study conducted by Genfit

NATIVE: a phase III enabling study

Trial design

Principal investigators

- Prof. Francque (Antwerp University, Belgium) and Prof. Abdelmalek (Duke University, USA)

Inclusion criteria

- Severe patients with an inflammation and ballooning score of 3 or 4
- Steatosis score ≥ 1 and fibrosis score < 4 (no cirrhosis)

Randomisation

- 1/1/1, stratification on T2DM patients
- Study powered with 75 patients per group
- Central reading

Clinicaltrials.gov identifier

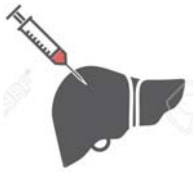
- NCT03008070

225 patients treated for 24 week + 4 week safety follow-up

Double blind randomized placebo controlled

Screening

- Liver biopsy



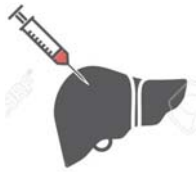
Placebo, 75 patients

Lanifibranor, 800 mg once daily, 75 patients

Lanifibranor, 1200 mg once daily, 75 patients

End of treatment

- Liver biopsy



Primary and key secondary endpoints

- Decrease from baseline ≥ 2 points of the inflammation and ballooning score without worsening of fibrosis
- Decrease of at least 2 points in NAS
- Resolution of NASH (to NAFLD: steatosis ± mild inflammation)
- Change in fibrosis score, liver enzymes, inflammatory markers, glucose metabolism parameters, plasma lipids parameters, adiponectin, …
- Safety

More information on: http://www.native-trial.com/ ; clinicaltrials.gov identifier: NCT03008070

Lanifibranor: differentiated potential compared to phase III programs to address all features of NASH in safe and efficacious manner

	Lanifibranor	Ocaliva	Cenicriviroc	Resmetirom	Aramchol
	inventiva	Intercept	Allergan	Madrigal Pharmaceuticals	Galmed Pharmaceuticals
Insulino-resistance	✓	✗	✗	✗	✗
Steatosis	✓	✗	✗	✓	✓
Necro-inflammation	✓	✗	✗	✓	Unclear
Fibrosis	✓	✓	✓	Unclear	✗

Recent and upcoming key milestones

Lanifibranor

- Results: phase IIb NASH - **June 2020**

Odiparcil

- ☑ Positive results of the phase IIa in MPS VI
- Launch of a Phase Ib/II clinical trial of odiparcil in a pediatric population with MPS VI
- Initiate a Phase IIa extension study in patients who completed the prior phase IIa trial

ABBV-157

abbvie

- ☑ ABBV-157 milestone received for the first psoriatic patient treated: **3,5M€ in Q4 2019**
- ABBV-157 clinical POC

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