Lanifibranor in Nonalcoholic Steatohepatitis (NASH)

NATIVE Phase IIb Topline Results

June 16, 2020
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NATIVE Phase IIb Webcast | June 2020
Today’s speakers

Frédéric Cren, MA/MBA, Chairman, CEO and cofounder

Pierre Broqua, Ph.D., CSO and cofounder

Marie-Paule Richard, MD, CMO

Prof. Sven Francque, MD
University Hospital Antwerp, Principal Investigator of NATIVE trial

Prof. Manal Abdelmalek, MD
Division of Gastroenterology and Hepatology at Duke University, Principal Investigator of NATIVE trial
Highlights of topline results

► **Lanifibranor (1,200 mg) met the primary endpoint** with a statistically significant reduction **after 6 months of treatment** of the Steatosis Activity Fibrosis score (SAF), which combines assessments of hepatocellular inflammation and ballooning, with no worsening of fibrosis in the Intention To Treat (ITT)\(^1\) and Per Protocol (PP)\(^2\) populations

► **Lanifibranor also met key secondary endpoints** including NASH resolution with no worsening of fibrosis and, at the 1,200 mg dose, improvement of liver fibrosis with no worsening of NASH in both ITT and PP populations

► **Lanifibranor is the first drug candidate to achieve statistically significant effects on the FDA and EMA primary endpoints relevant for seeking accelerated approval:**
  - NASH resolution with no worsening of fibrosis
  - Improvement of fibrosis with no worsening of NASH

► **Lanifibranor continued to show a favorable tolerability profile**

► Positive topline results support Inventiva’s decision to move forward with the clinical development of lanifibranor and **enter into pivotal Phase III development**

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\(^1\) ITT: includes all patients randomized in the trial.

\(^2\) PP: includes all patients with paired biopsies and without deviation impacting efficacy assessment.
**Lanifibranor: the only pan-PPAR agonist in clinical development for the treatment of NASH**

Moderate and balanced pan-PPAR agonist activity

- Differentiated chemical structure
- Once daily oral administration
- Composition of matter patent granted in 55 countries and method of use patent granted in the US, China and in the EU: limit of exclusivity in the US is 2035
- FAST Track designation granted by FDA

<table>
<thead>
<tr>
<th>Compound</th>
<th>PPARα EC50 (nM)</th>
<th>PPARδ EC50 (nM)</th>
<th>PPARγ EC50 (nM)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lanifibranor(1)</td>
<td>1630</td>
<td>850</td>
<td>230</td>
</tr>
<tr>
<td>Fenofibrate</td>
<td>2400</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Pioglitazone</td>
<td>-</td>
<td>-</td>
<td>263</td>
</tr>
<tr>
<td>Rosiglitazone</td>
<td>-</td>
<td>-</td>
<td>13</td>
</tr>
<tr>
<td>Elafibranor(2)</td>
<td>10</td>
<td>100</td>
<td>-</td>
</tr>
<tr>
<td>Seladelpar(3)</td>
<td>-</td>
<td>2</td>
<td>-</td>
</tr>
</tbody>
</table>

Results justifying a NASH development

- Effects observed 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 tolerability profile

- 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 trial with 47 TD2M patients
- Approximately 250 patients treated for 24 or 48 weeks in Inventiva’s completed Phase IIb clinical trials
- In connection with these trials, lanifibranor has undergone a total of 7 DSMB reviews without recommendations of protocol change

(1) Conducted by Abbott prior to our founding; (2) Including 125 healthy volunteers in the phase I conducted by Abbott prior to our founding.
Trial design
Clinicaltrials.gov identifier: NCT03008070

Screening
- Liver biopsy

24-week treatment + 4-week follow-up
Double blind, randomized, placebo-controlled

Placebo
- Lanifibranor, 800 mg once daily
- Lanifibranor, 1200 mg once daily

End of treatment
- Liver biopsy

- Randomisation 1/1/1
- Stratification on type 2 diabetes mellitus (T2DM)

Patient population | # patients | Definition
--- | --- | ---
Safety / Intention-to-Treat (ITT) | 247 | Patients randomized having received at least one dose of lanifibranor/placebo
Per Protocol (PP) | 194 | Patients with paired biopsies and without deviation impacting efficacy results

Main inclusion criteria: patients with biopsy-proven NASH confirmed by central reader having Steatosis-Activity-Fibrosis (SAF) scores of 1-3 for steatosis, 3-4 for activity, and <4 for fibrosis

More information on: http://www.native-trial.com/
### 247 patients randomized in 71 sites worldwide

<table>
<thead>
<tr>
<th>Country</th>
<th>Patients randomized</th>
</tr>
</thead>
<tbody>
<tr>
<td>Europe</td>
<td>183 (74%)</td>
</tr>
<tr>
<td>US</td>
<td>36 (15%)</td>
</tr>
<tr>
<td>Australia</td>
<td>13 (5%)</td>
</tr>
<tr>
<td>Canada</td>
<td>8 (3%)</td>
</tr>
<tr>
<td>Mauritius</td>
<td>7 (3%)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>247 (100%)</strong></td>
</tr>
</tbody>
</table>

#### 17 countries worldwide (number of sites having randomized at least 1 patient)
- Europe: Austria (1), Belgium (5), Bulgaria (5), Czech Republic (3), France (13), Germany (5), Italy (4), Poland (3), Slovenia (1), Spain (4), Switzerland (2), United Kingdom (3)
- North America: United States (12), Canada (4)
- Australia (5)
- Mauritius (1)

- 4 sites in Canada
- 12 sites in the United States
- 49 sites in Europe
- 5 sites in Australia
- 1 site in Mauritius
- 4 sites in Canada
- 12 sites in the United States
- 49 sites in Europe
- 5 sites in Australia
- 1 site in Mauritius

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Efficacy endpoints

Primary endpoint

- Decrease from baseline to week 24 of at least 2 points of inflammation and ballooning and no worsening of fibrosis (as measured by SAF activity score)

Secondary endpoints

- Resolution of NASH and no worsening of fibrosis
- Improvement of fibrosis by at least 1 stage and no worsening of NASH
- Decrease from baseline to week 24 of at least 2 points of the NAS CRN score and no worsening of fibrosis
- Resolution of NASH and improvement of fibrosis by at least 1 stage
- Change in glucose metabolism parameters (fasting glucose, insulin, HOMA index, HbA1c, …)
- Change in liver enzymes tests (ALT, AST, GGT, Alkaline Phosphatase, Total Bilirubin)
- Change in main plasma lipid parameters (TC, HDL-C, calculated LDL-C, TG,…)

Other outcome measures

- Change in inflammatory markers (fibrinogen, hs-CRP, alpha2 macroglobulin, haptoglobin,…)
- Change in fibrosis markers (TIMP-1, TIMP-2, Hyaluronic acid, P3NP, NFS, FIB-4 score, ELF score, Pro-C3,…)

The severity of hepatocellular ballooning and inflammation is a strong predictor for the presence of hepatic fibrosis and the risk for fibrosis progression.

NATIVE primary endpoint is a reduction of ≥ 2 points of the SAF activity score, which excludes steatosis and focuses on inflammation and ballooning.

Other key endpoints assess disease progression using both biopsy scoring measurements: SAF and NAS.

### SAF

**Steatosis-Activity-Fibrosis**

<table>
<thead>
<tr>
<th>Steatosis</th>
<th>Activity</th>
<th>Fibrosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 - 3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0 - 2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0 - 4</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### NAS

**NAFLD Activity Score**

<table>
<thead>
<tr>
<th>Steatosis</th>
<th>Activity</th>
<th>Inflammation</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 - 3</td>
<td></td>
<td>0 - 3</td>
</tr>
<tr>
<td>0 - 2</td>
<td></td>
<td>0 - 3</td>
</tr>
</tbody>
</table>

**Fibrosis improvement**

≥ 2 points reduction of NAS score

NASH resolution

Decrease of ≥ 2 points of SAF activity score
Patient disposition (N = 247)

247 patients randomised and treated

Placebo
N = 81

- 74 (91%) patients completed the 24-week treatment
- 7 (9%) patients prematurely withdrawn:
  - Adverse events (n=3)
  - Withdrawal by patient (n=2)
  - Forbidden concomitant medication (n=2)

Lanifibranor 800 mg/day
N = 83

- 77 (93%) patients completed the 24-week treatment
- 6 (7%) patients prematurely withdrawn:
  - Adverse events (n=3)
  - Lost to follow-up (n=1)
  - Withdrawal by patient* (n=1)
  - Non-compliance (n=1)

Lanifibranor 1200 mg/day
N = 83

- 77 (93%) patients completed the 24-week treatment
- 6 (7%) patients prematurely withdrawn:
  - Adverse events (n=3)
  - Lost to follow-up (n=1)
  - Withdrawal by patient (n=2)

* and adverse event as secondary reason
# Patient Baseline Demographics and Characteristics (I/II)
## ITT (N = 247)

<table>
<thead>
<tr>
<th>Parameters (unit)</th>
<th>Placebo - N = 81</th>
<th>Lanifibranor 800 mg/day - N = 83</th>
<th>Lanifibranor 1200 mg/day - N = 83</th>
<th>Overall - N = 247</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>n (%)</strong> or <strong>mean ± SD</strong></td>
<td><strong>Female</strong></td>
<td><strong>Age (years)</strong></td>
<td><strong>White</strong></td>
<td><strong>Weight (kg)</strong></td>
</tr>
<tr>
<td><strong>n (%)</strong> or <strong>mean ± SD</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Demographics</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Female</strong></td>
<td>41 (51%)</td>
<td>54 (65%)</td>
<td>49 (59%)</td>
<td>144 (58%)</td>
</tr>
<tr>
<td><strong>Age (years)</strong></td>
<td>53.4 ± 13.1</td>
<td>55.0 ± 10.4</td>
<td>52.2 ± 13.8</td>
<td>53.6 ± 12.5</td>
</tr>
<tr>
<td><strong>White</strong></td>
<td>74 (91%)</td>
<td>80 (96%)</td>
<td>78 (94%)</td>
<td>232 (94%)</td>
</tr>
<tr>
<td><strong>Weight (kg)</strong></td>
<td>95.1 ± 17.3</td>
<td>91.6 ± 19.3</td>
<td>93.0 ± 19.9</td>
<td>93.2 ± 18.9</td>
</tr>
<tr>
<td><strong>Body Mass Index (kg/m²)</strong></td>
<td>32.8 ± 5.1</td>
<td>32.5 ± 5.5</td>
<td>33.3 ± 5.5</td>
<td>32.9 ± 5.4</td>
</tr>
<tr>
<td><strong>Type 2 diabetes</strong></td>
<td>35 (43%)</td>
<td>33 (40%)</td>
<td>35 (42%)</td>
<td>103 (42%)</td>
</tr>
<tr>
<td><strong>Liver biopsy characteristics</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>SAF Activity score (inflammation + ballooning)</strong></td>
<td>3.3 ± 0.5</td>
<td>3.2 ± 0.5</td>
<td>3.3 ± 0.5</td>
<td>3.3 ± 0.5</td>
</tr>
<tr>
<td><strong>NAFLD Activity Score (NAS) ≥6</strong></td>
<td>56 (69.1%)</td>
<td>63 (75.9%)</td>
<td>61 (73.5%)</td>
<td>180 (72.9%)</td>
</tr>
<tr>
<td><strong>Fibrosis stage F2/F3</strong></td>
<td>57 (70.4%)</td>
<td>68 (81.9%)</td>
<td>63 (75.9%)</td>
<td>188 (76.1%)</td>
</tr>
</tbody>
</table>
### Patient Baseline Demographics and Characteristics (II/II)

**ITT (N = 247)**

<table>
<thead>
<tr>
<th>Parameters (unit)</th>
<th>Placebo N = 81</th>
<th>Lanifibranor 800 mg/day N = 83</th>
<th>Lanifibranor 1200 mg/day N = 83</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Liver enzymes</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alanine aminotransferase, ALT (UI/L)</td>
<td>56.9 ± 31.6</td>
<td>64.1 ± 41.4</td>
<td>63.6 ± 43.4</td>
</tr>
<tr>
<td>Aspartate aminotransferase, AST (UI/L)</td>
<td>43.3 ± 24.1</td>
<td>53.9 ± 43.4</td>
<td>43.9 ± 24.8</td>
</tr>
<tr>
<td>Gamma glutamyl transferase, GGT (UI/L)</td>
<td>67.9 ± 80.4</td>
<td>101.6 ± 146.1</td>
<td>67.1 ± 93.1</td>
</tr>
<tr>
<td><strong>Plasma lipids levels</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HDL-Cholesterol (mmol/L)</td>
<td>1.2 ± 0.3</td>
<td>1.3 ± 0.3</td>
<td>1.2 ± 0.3</td>
</tr>
<tr>
<td>Triglycerides (mmol/L)</td>
<td>2.0 ± 0.8</td>
<td>1.9 ± 0.9</td>
<td>2.0 ± 0.9</td>
</tr>
<tr>
<td><strong>Glucose metabolism for diabetic patients (n= 103)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fasting Glucose (mmol/L)</td>
<td>6.9 ± 2.0</td>
<td>7.3 ± 2.2</td>
<td>6.6 ± 1.2</td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td>6.5 ± 0.7</td>
<td>6.7 ± 0.8</td>
<td>6.6 ± 0.7</td>
</tr>
<tr>
<td>Insulin (pmol/L)</td>
<td>222.7 ± 186.5</td>
<td>246.3 ± 213.4</td>
<td>278.5 ± 233.5</td>
</tr>
</tbody>
</table>
Dose-dependent and statistically significant (1200 mg) reduction of 2 points of inflammation and ballooning (SAF Activity Score) and no worsening of fibrosis

Primary Efficacy Endpoint

ITT Population (N = 247)

<table>
<thead>
<tr>
<th>Dose</th>
<th>Placebo</th>
<th>Lanifibranor 800 mg</th>
<th>Lanifibranor 1200 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>% patients</td>
<td>27%</td>
<td>41%</td>
<td>49%</td>
</tr>
<tr>
<td>(N= 81)</td>
<td>(N= 83)</td>
<td>(N= 83)</td>
<td></td>
</tr>
</tbody>
</table>

Per Protocol Population (N = 194)

<table>
<thead>
<tr>
<th>Dose</th>
<th>Placebo</th>
<th>Lanifibranor 800 mg</th>
<th>Lanifibranor 1200 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>% patients</td>
<td>34%</td>
<td>51%</td>
<td>55%</td>
</tr>
<tr>
<td>(N= 62)</td>
<td>(N= 63)</td>
<td>(N= 69)</td>
<td></td>
</tr>
</tbody>
</table>

p=0.004*  
p=0.061  
p=0.015*  
p=0.058

* Statistically significant in accordance to the statistical analysis plan (SAP)

Lanifibranor (1200 mg) **met** the primary endpoint in both ITT and PP populations

Primary efficacy endpoint: Response is defined as a decrease from baseline to week 24 of at least 2 points of the SAF Activity score (SAF-A) and no worsening of the CRN Fibrosis score (CRN-F). No worsening means that the score remains stable or decreases.
Dose-dependent and statistically significant results in resolution of NASH and no worsening of fibrosis

Secondary endpoint

ITT Population (N = 247)

Per Protocol Population (N = 194)

* Statistically significant in accordance to the statistical analysis plan (SAP)

- Both lanifibranor dose groups met resolution of NASH and no worsening of fibrosis in both ITT and PP populations
- 49% of patients treated with lanifibranor 1200mg daily in the PP population had their NASH resolved

Resolution of NASH and no worsening of fibrosis at week 24: CRN-I = 0 or 1, CRN-B = 0 and no worsening of CRN-F from baseline.
Dose-dependent and statistically significant results in resolution of NASH and no worsening of fibrosis in F2/F3 patients in both ITT and PP populations

Secondary endpoint in F2/F3 patients

**ITT Population in F2/F3 (N = 188)**

- Placebo: 9% (N = 57)
- Lanifibranor 800 mg: 34% (N = 68)
- Lanifibranor 1200 mg: 44% (N = 63)

**Per Protocol Population in F2/F3 (N = 149)**

- Placebo: 11% (N = 45)
- Lanifibranor 800 mg: 40% (N = 53)
- Lanifibranor 1200 mg: 51% (N = 51)

* Statistically significant in accordance to the statistical analysis plan (SAP)

➤ In the ITT population, approximately four times and five times more patients in the 800mg/day dose and 1200mg/day group respectively met the secondary endpoint compared to placebo.

Resolution of NASH and no worsening of fibrosis at week 24: CRN-I = 0 or 1, CRN-B = 0 and no worsening of CRN-F from baseline.
Dose-dependent and statistically significant (1200 mg) improvement of fibrosis and no worsening of NASH

Secondary endpoint

**ITT Population (N = 247)**

<table>
<thead>
<tr>
<th>Dose</th>
<th>% Patients</th>
<th><em>p</em> Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>24%</td>
<td>p=0.53</td>
</tr>
<tr>
<td>Lanifibranor 800 mg</td>
<td>28%</td>
<td>p=0.011*</td>
</tr>
<tr>
<td>Lanifibranor 1200 mg</td>
<td>42%</td>
<td></td>
</tr>
</tbody>
</table>

**Per Protocol Population (N = 194)**

<table>
<thead>
<tr>
<th>Dose</th>
<th>% Patients</th>
<th><em>p</em> Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>29%</td>
<td>p=0.75</td>
</tr>
<tr>
<td>Lanifibranor 800 mg</td>
<td>32%</td>
<td></td>
</tr>
<tr>
<td>Lanifibranor 1200 mg</td>
<td>46%</td>
<td></td>
</tr>
</tbody>
</table>

* Statistically significant in accordance to the statistical analysis plan (SAP)

- Lanifibranor 1200 mg group met improvement of fibrosis and no worsening of NASH in both ITT and PP populations
- 46% of patients treated with lanifibranor 1200mg daily in the PP population had their fibrosis reduced in 6 months

*Statistically significant in accordance to the statistical analysis plan (SAP)*
Dose-dependent and statistically significant results on both resolution of NASH and fibrosis improvement

Secondary endpoint

**ITT Population (N = 247)**

- **Lanifibranor 800 mg**: 21%
- **Lanifibranor 1200 mg**: 31%
- **Placebo**: 7%

**Per Protocol Population (N = 194)**

- **Lanifibranor 800 mg**: 24%
- **Lanifibranor 1200 mg**: 33%
- **Placebo**: 10%

* Statistically significant in accordance to the statistical analysis plan (SAP)

- **Both lanifibranor dose groups** met resolution of NASH and fibrosis improvement in both ITT and PP populations

- **In the ITT population**, three times and four times more patients in the 800mg/day dose and 1200mg/day group respectively met the secondary endpoint compared to placebo

Resolution of NASH and Improvement of liver fibrosis ≥ 1 stage at week 24: CRN-I = 0 or 1, CRN-B = 0 and Improvement of CRN-F ≥ 1 stage.
Statistically significant decrease in liver enzymes

Other secondary endpoints in ITT (N = 247)

Absolute change from baseline in ALT

Mean absolute change (UI/L)

Placebo Lanifibranor 800mg Lanifibranor 1200mg

Mean absolute change from baseline in AST

Mean absolute change (UI/L)

Placebo Lanifibranor 800mg Lanifibranor 1200mg

Absolute change from baseline in GGT

Mean absolute change (U/L)

Placebo Lanifibranor 800mg Lanifibranor 1200mg

* p<0.01  **p<0.001

Statistically significant decrease of ALT, AST and GGT in both lanifibranor dose groups observed beginning after 4 weeks
Statistically significant change in HDL-cholesterol and triglycerides

Other secondary endpoints in ITT (N = 247)

Absolute change from baseline in HDL-C

Absolute change from baseline in triglycerides

* p<0.01  **p<0.001

No change in LDL-cholesterol
Statistically significant reductions of fasting glucose and insulin, HbA1c in type 2 diabetes (T2DM) patients with NASH

Secondary endpoints in T2DM patients with NASH (N = 103)

Absolute change from baseline in HbA1c

Absolute change from baseline in fasting glucose

Absolute change from baseline in insulin at W24

Lanifibranor improves insulin sensitivity and glycemic control in NASH patients

**p<0.001
### Lanifibranor: a continued favorable tolerability profile (I/II)

**Safety population N = 247**

<table>
<thead>
<tr>
<th>N (%) patients reporting Adverse Event (AE)</th>
<th>Placebo (N = 81)</th>
<th>800 mg (N = 83)</th>
<th>1200 mg (N = 83)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Any Treatment-Emergent AE (TEAE)</strong></td>
<td>50 (61.7%)</td>
<td>59 (71.1%)</td>
<td>62 (74.7%)</td>
</tr>
<tr>
<td>- Drug-related TEAE</td>
<td>19 (23.5%)</td>
<td>25 (30.1%)</td>
<td>23 (27.7%)</td>
</tr>
<tr>
<td><strong>Any TEAE leading to drug withdrawal</strong></td>
<td>3 (3.7%)</td>
<td>4 (4.8%)</td>
<td>3 (3.6%)</td>
</tr>
<tr>
<td>- Drug-related TEAE leading to drug withdrawal</td>
<td>2 (2.5%)</td>
<td>1 (1.2%)</td>
<td>2 (2.4%)</td>
</tr>
<tr>
<td><strong>Any Serious TEAE</strong></td>
<td>3 (3.7%)</td>
<td>3 (3.6%)</td>
<td>7 (8.4%)</td>
</tr>
<tr>
<td>- Drug-related Serious TEAE</td>
<td>2 (2.5%)</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

(1) One patient with moderate diarrhea  
(2) One patient with mild cardiac failure; one patient with mild diarrhea, abdominal pain, dizziness  
(3) 2 SUSARs: one patient with mild cardiac failure; one patient with moderate urticaria

▶ Consistent with known insulin sensitizing pharmacology, a mean weight increase from baseline of 2.4 kg (2.6%) at the 800 mg/day dose and 2.7 kg (3.1%) at the 1200 mg/day dose was observed.

<table>
<thead>
<tr>
<th>Peripheral edema</th>
<th>Placebo (N = 81)</th>
<th>800 mg (N = 83)</th>
<th>1200 mg (N = 81)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2 (2.5%)</td>
<td>5 (6.0%)</td>
<td>7* (8.4%)</td>
</tr>
<tr>
<td>- Drug-related peripheral edema</td>
<td>-</td>
<td>2 (2.4%)</td>
<td>2 (2.4%)</td>
</tr>
</tbody>
</table>

* One AE of severe intensity
**Lanifibranor: a continued favorable tolerability profile (II/II)**

*Safety population N = 247*

The table below summarizes the patients reporting treatment-emergent serious adverse events (SAEs) in the placebo and two treatment groups:

<table>
<thead>
<tr>
<th>Patients reporting treatment-emergent serious AE (SAE); N (%)</th>
<th>Placebo (N = 81)</th>
<th>800 mg (N = 83)</th>
<th>1200 mg (N = 83)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total</strong></td>
<td>3 (3.7%)</td>
<td>3 (3.6%)</td>
<td>7 (8.4%)</td>
</tr>
</tbody>
</table>

**Treatment-Emergent Serious AE linked to biopsy procedure**

<table>
<thead>
<tr>
<th>Event</th>
<th>Placebo (N = 81)</th>
<th>800 mg (N = 83)</th>
<th>1200 mg (N = 83)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Post-procedural haematoma/haemorrhage</td>
<td>-</td>
<td>1 (1.2%)</td>
<td>1 (1.2%)</td>
</tr>
<tr>
<td>Post-procedural pain</td>
<td>-</td>
<td>-</td>
<td>1 (1.2%)</td>
</tr>
<tr>
<td>Pneumobilia (post-procedural)</td>
<td>-</td>
<td>-</td>
<td>1 (1.2%)</td>
</tr>
</tbody>
</table>

**Other Treatment-Emergent Serious AE**

<table>
<thead>
<tr>
<th>Event</th>
<th>Placebo (N = 81)</th>
<th>800 mg (N = 83)</th>
<th>1200 mg (N = 83)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wrist fracture</td>
<td>1 (1.2%)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Angina unstable</td>
<td>-</td>
<td>-</td>
<td>1 (1.2%)</td>
</tr>
<tr>
<td>Cardiac failure</td>
<td>1 (1.2%)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Gastroenteritis</td>
<td>-</td>
<td>-</td>
<td>1 (1.2%)</td>
</tr>
<tr>
<td>Pyelonephritis</td>
<td>-</td>
<td>-</td>
<td>1 (1.2%)</td>
</tr>
<tr>
<td>Pancreatitis</td>
<td>-</td>
<td>1 (1.2%)</td>
<td>-</td>
</tr>
<tr>
<td>Undifferentiated connective tissue disease</td>
<td>-</td>
<td>1 (1.2%)</td>
<td>-</td>
</tr>
<tr>
<td>Urticaria</td>
<td>1 (1.2%)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Foot operation</td>
<td>-</td>
<td>-</td>
<td>1 (1.2%)</td>
</tr>
</tbody>
</table>
Lanifibranor NATIVE results and other oral NASH drug candidates (I/II)

Phase II results of orally available drug candidates: NASH resolution without worsening of fibrosis

No head-to-head clinical trials have been conducted; results obtained from different trials, with different designs, endpoints and patient populations. Results may not be comparable.

Source: Lanifibranor native results 1200 mg/day, ITT population: ocaliva 25mg ; Farnesoid X nuclear receptor ligand obeticholic acid for non-cirrhotic, non-alcoholic steatohepatitis (FLINT): a multicentre, randomised, placebo-controlled trial The Lancer November 6 2014; elafibranor 120mg; Ratziu et al, Gastroenterology 2016; 150:1147-1159 ; resmetirom 80mg ± 20mg: Harrison et al, Lancet 2019 ; S0140-6736(19) 32517-6; Aramchol 600mg :AASLD 2018 presentation

NATIVE Phase IIb Webcast | June 2020

**Phase II results of orally available drug candidates: NASH resolution without worsening of fibrosis**

- **Lanifibranor NATIVE**
  - **Phase II**
    - **6 months**: 45%
    - **18 months**: 19%
  - **N = 247**
  - **P = <0.001**

- **Ocaliva**
  - **Phase II**
    - **12 months**: 21.3%
    - **18 months**: 13.3%
  - **N = 283**
  - **P = 0.08**

- **Aramchol**
  - **Phase II**
    - **12 months**: 16.7%
  - **N = 247**
  - **P = 0.051**

- **Elafibranor**
  - **Phase II**
    - **12 months**: 19.0%
  - **N = 276**
  - **P = 0.045**

- **Resmetirom**
  - **Phase II**
    - **9 months**: 24.7%
  - **N = 125**
  - **P = 0.03**
Lanifibranor NATIVE results and other oral NASH drug candidates (II/II)

Phase II results of orally available drug candidates: fibrosis improvement without worsening of NASH\(^{(1)}\)

- **Lanifibranor**
  - **N** = 247
  - **N** = 283
  - **P** = 0.011
  - **P** = 0.004

- **Ocaliva**
  - **Phase II 6 months**
  - **Phase II 18 months**
  - **P** = 0.011

- **Elafibranor**
  - **Phase II 9 months**
  - **Phase II 12 months**
  - **N/A**
  - **N** = 276
  - **P** = 0.21

- **Aramchol**
  - **Phase II 12 months**
  - **29.5%**
  - **23.5%**

- **Resmetirom**
  - **Phase II 9 months**
  - **28.8%**
  - **No stats reported**

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**No head-to-head clinical trials have been conducted; results obtained from different trials, with different designs, endpoints and patient populations. Results may not be comparable.**

Source: lanifibranor native results 1200 mg/day, ITT population; ocaliva 25mg: Farnesoid X nuclear receptor ligand obeticholic acid for non-cirrhotic, non-alcoholic steatohepatitis (FLINT): a multicentre, randomised, placebo-controlled trial The Lancet November 6 2014; elafibranor 120mg: Ratziu et al, Gastroenterology 2016; 150:1147-1159 ; resmetirom 80mg ± 20mg: Harrison et al, Lancet 2019 ; S0140-6736(19)32517-6; Aramchol 600mg :AASLD 2018 presentation.
Conclusion

► Lanifibranor (1,200 mg) met the primary endpoint with a statistically significant reduction after 6 months of treatment of the Steatosis Activity Fibrosis score (SAF), which combines assessments of hepatocellular inflammation and ballooning, with no worsening of fibrosis in the Intention To Treat (ITT)\(^1\) and Per Protocol (PP)\(^2\) populations

► Lanifibranor also met key secondary endpoints including NASH resolution with no worsening of fibrosis and, at the 1,200 mg dose, improvement of liver fibrosis with no worsening of NASH in both ITT and PP populations

► Lanifibranor is the first drug candidate to achieve statistically significant effects on the FDA and EMA primary endpoints relevant for seeking accelerated approval:
  ► NASH resolution with no worsening of fibrosis
  ► Improvement of fibrosis with no worsening of NASH

► Lanifibranor continued to show a favorable tolerability profile

► Positive topline results support Inventiva’s decision to move forward with the clinical development of lanifibranor and enter into pivotal Phase III development

\(^1\) ITT: includes all patients randomized in the trial.
\(^2\) PP: includes all patients with paired biopsies and without deviation impacting efficacy assessment.
Lanifibranor: NASH key milestones

- Finalization of Phase III synopsis and protocol: ongoing
- End of Phase IIb meeting with FDA: expected in Q4 2020
- Scientific advice meeting with EMA: expected in Q4 2020
- Finalization of Phase II trial in NAFLD patients with TD2M conducted by Pr. Cusi
- Launch of pivotal Phase III trial in NASH
Q & A