Developing breakthrough therapies in systemic sclerosis, NASH and mucopolysaccharidosis

Corporate Presentation
January 2019
This document has been prepared by Inventiva (the "Company") solely for the purpose of this presentation. This presentation includes only summary information and does not purport to be comprehensive. Any information in this presentation, whether from internal or from external sources, is purely indicative and has no contractual value. The information contained in this presentation are provided as at the date of this presentation. Certain information included in this presentation and other statements or materials published or to be published by the Company are not historical facts but are forward-looking statements. The forward-looking statements are based on current beliefs, expectations and assumptions, including, without limitation, assumptions regarding present and future business strategies and market in which the Company operates, and involve known and unknown risk, uncertainties and other factors, which may cause actual results, performance or achievements, or industry results or other events, to be materially different from those expressed or implied by these forward-looking statements. These risks and uncertainties include those discussed or identified under Chapter “Risk factors” in the Company’s registration document (document de reference) filed with the French Financial markets authority (AMF – Autorité des marchés financiers), available on the Company’s website (www.inventivapharma.com) and on the website of the AMF. The Company may not actually achieve the plans, intents or expectations disclosed in its forward-looking statements and you should not place undue reliance on the forward-looking statements contained herein. There can be no assurance that the actual results of the Company’s development activities and results of operations will not differ materially from the Company’s expectations. Factors that could cause actual results to differ from expectations include, among others, the Company’s ability to develop safe and effective products, to achieve positive results in clinical trials, to obtain marketing approval and market acceptance for its products, and to enter into and maintain collaborations; as well as the impact of competition and technological change; existing and future regulations affecting the Company’s business; and the future scope of the Company’s patent coverage or that of third parties.

The information contained in this presentation has not been subject to independent verification. No representation or warranty, express or implied, is made by the Company or any of its affiliates, advisors, representatives, agents or employees as to, and no reliance should be placed on, the fairness, accuracy, completeness or correctness of the information, or opinions contained herein. Neither the Company, nor any of its respective affiliates, advisors, representatives, agents or employees, shall bear any responsibility or liability whatsoever (for negligence or otherwise) for any loss howsoever arising from any use of this presentation or its contents or otherwise arising in connection with this presentation. Such information is subject to modification at any time, including without limitation as a result of regulatory changes or changes with respect to market conditions, and neither the Company, nor any of its affiliates, advisors, representatives, agents or employees, shall, nor has any duty to, update you.
Inventiva investment 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 three high value indications
  - **Lanifibranor** – only pan-PPAR agonist in clinical development, Phase IIb data in SSc and NASH due early 2019 and H1 2020 respectively
  - **Odiparcil** – first orally available therapy for MPS, Phase IIa data due H2 2019

- **State of the art R&D capabilities** including wholly owned ‘pharma scale’ discovery facilities

- Portfolio underpinned by **discovery engine** focused on nuclear receptors, transcription factors and epigenetic targets with a **240,000** compound library, **60%** of which are proprietary

- **Compelling early stage pipeline** leveraging power of discovery engine in fibrotic disease and oncology, supported by validating partnerships with AbbVie and Boehringer Ingelheim

- **Strong balance sheet** and **experienced senior management** team with a track record of operational and scientific excellence
Management team with extensive experience across all stages of drug development and commercialization

Frédéric Cren, MA/MBA, CEO and Co-Founder
- Wide expertise within the areas of research, development, marketing, strategy and commercial operations
- Held senior positions at Abbott, Fournier, Solvay Pharma and The Boston Consulting Group
- Former member of both Fournier and Solvay Pharma Executive Committees

Pierre Broqua, Ph.D., CSO and Co-Founder
- Has successfully managed numerous research programs leading to the discovery, development and commercialization of innovative compounds, including lanifibranor and Ferring’s GnRH antagonist Degarelix/Firmagon®
- Held several senior research positions at Fournier, Solvay Pharma and Abbott

Jean Volatier, MA, CFO
- Started his career with PwC in Paris and Philadelphia
- Former Head of controlling at URGO & Financial Director International Operations of Fournier
- Held various positions as CFO with Soufflet and Naos groups

Marie-Paule Richard, MD, CMO
- Long and diverse international experience acquired with large pharmaceutical organizations such as GSK, Aventis, Sanofi Pasteur as well as biotech in CMO roles
- Former CMO of Belgium biotech Tigenix, recently acquired by Takeda
- Joined Inventiva in mid-October to prepare for former CMO JL Abitbol retirement planned April 2019
Inventiva – evolving into a late stage biotech company targeting multiple high value indications
Validated oral small molecule-focused discovery engine targeting nuclear receptors, transcription factors and epigenetic modulation

- Extensive library of pharmacologically relevant molecules
  - Library includes ~240,000 compounds of which 60% proprietary
- Wholly-owned pharma-like R&D facilities
  - 129,000 square foot (12,000m²) with comprehensive chemistry, biology and DMPK laboratories
- Deep expertise and experience in nuclear receptors, transcription factors and epigenetic modulation
- Strong scientific team of ~90 people
  - 75% of the team has been working together for more than 15 years

Power of discovery engine underpins deep pipeline of clinical and discovery stage assets
### Deep pipeline approaching major near term value inflection points

<table>
<thead>
<tr>
<th>Candidate / Program</th>
<th>Indication</th>
<th>Discovery</th>
<th>IND Enabling</th>
<th>Phase I</th>
<th>Phase II</th>
<th>Phase III</th>
<th>Commercial Rights</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lanifibranor</td>
<td>SSc</td>
<td>pan-PPAR</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Pivotal Phase IIb results expected in Q1 2019</td>
</tr>
<tr>
<td>Lanifibranor</td>
<td>NASH</td>
<td>pan-PPAR</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Pivotal Phase IIb results expected in H1 2020</td>
</tr>
<tr>
<td>Odiparcil</td>
<td>MPS VI</td>
<td>GAG clearance</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Phase IIa results expected in H2 2019</td>
</tr>
<tr>
<td>ABBV-157</td>
<td>Moderate to severe psoriasis</td>
<td>RORγ</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Phase I ongoing</td>
</tr>
<tr>
<td>Hippo</td>
<td>Non-small cell lung cancer and mesothelioma</td>
<td>YAP/TEAD</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Candidate Selection</td>
</tr>
<tr>
<td>TGF-β</td>
<td>Idiopathic pulmonary fibrosis (IPF)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Lead Optimization(1)</td>
</tr>
</tbody>
</table>

(1) Lead optimization means refining molecules in advance of selecting candidates
Strong cash position and shareholder base

Key financials

<table>
<thead>
<tr>
<th>ISIN code</th>
<th>FR0013233012</th>
</tr>
</thead>
<tbody>
<tr>
<td>Market</td>
<td>Euronext Paris</td>
</tr>
<tr>
<td>Shares outstanding</td>
<td>22,257,277</td>
</tr>
<tr>
<td>Market cap (January 2 2019)</td>
<td>€125m</td>
</tr>
<tr>
<td>Cash position (June 30 2018)</td>
<td>€75.9m compared to €59.0m in December 2017. Successful €48.5m Euronext IPO (February 2017) and €35.5m private placement (April 2018)</td>
</tr>
<tr>
<td>Revenues in H1 2018 (June 30 2018)</td>
<td>€1.4m compared to €2.9m in H1 2017</td>
</tr>
<tr>
<td>R&amp;D expenditures in H1 2018 (June 30 2018)</td>
<td>€16.0m compared to €13.2m in H1 2017</td>
</tr>
</tbody>
</table>

Shareholder base

- Founders 43.9%
- BVF 15.0%
- Novo 8.8%
- Sofinnova 7.1%
- Employees & Others 3.1%
- Founders *Including Perceptive Advisors

Analyst coverage

<table>
<thead>
<tr>
<th>Jefferies</th>
<th>Peter Welford</th>
</tr>
</thead>
<tbody>
<tr>
<td>Société Générale</td>
<td>Delphine Le Louët</td>
</tr>
<tr>
<td>Gilbert Dupont</td>
<td>Jamila El Bougrini</td>
</tr>
<tr>
<td>Kepler Chevreux</td>
<td>Arsene Guekam</td>
</tr>
<tr>
<td>KBC</td>
<td>Lenny Van Steenhuyse</td>
</tr>
<tr>
<td>LifeSci Capital</td>
<td>Patrick Dolezal</td>
</tr>
</tbody>
</table>
Lanifibranor – Systemic Sclerosis (SSc) and Nonalcoholic Steatohepatitis (NASH)
Lanifibranor: only pan-PPAR agonist in clinical development for the treatment of fibrotic conditions

**Activity**
- Differentiated chemical structure with moderate and balanced pan-PPAR agonist activity (PPARα, PPARγ and PPARδ)
- Oral administration
- Anti-fibrotic, anti-inflammatory and beneficial metabolic effects observed in preclinical models
- Phase IIa trial demonstrated pan-PPAR agonist activity, supporting dose selection for NASH and SSc clinical trials

**Safety**
- Favorable safety profile demonstrated in 24-months rodent and 12-month monkey studies, highly differentiated from other PPAR compounds; first PPAR drug to receive EMA authorization to perform 12 month study in humans in parallel with long-term toxicological studies
- 125 healthy volunteers treated in Phase I trials and 47 patients treated in Phase IIa study
- ~170 patients treated for at least 24 weeks in ongoing Phase IIb trials; 5 positive DSMB reviews completed
- Safety profile established in Phase I and Phase IIa T2DM studies

**IP**
- Composition of matter patent granted in 53 countries: LOE August 2031 including 5-year extension
- Use patent granted in US covering several fibrotic diseases including NASH and SSc: LOE 2035
- Orphan Drug Designation granted in SSc in the US and EU

(1) Conducted by Abbott prior to our funding (2) LOE: Loss of exclusivity

Corporate Presentation | 2019

Non-confidential – Property of Inventiva | 10
The three PPAR isoforms have well established roles in fibrotic, inflammatory and metabolic processes.

- **FIBROSIS**
  - PPARγ
    - Fibroblast activation
    - Collagen production

- **INFLAMMATION**
  - PPARα, δ, γ
    - Macrophage cell response
    - Endothelial cell response

- **METABOLISM**
  - PPARα, δ, γ
    - HDL Cholesterol
    - Triglycerides

- **Pan-PPAR agonist**
  - Anti-fibrotic
  - Anti-inflammatory
  - Positive Metabolic Effects

- **INFLAMMATION**
  - Anti-inflammatory

- **METABOLISM**
  - Insulin Sensitivity

---

Corporate Presentation | 2019

Non-confidential – Property of Inventiva | 11
Lanifibranor is a differentiated pan-PPAR agonist with moderate and well balanced activity on the 3 PPAR isoforms

Lanifibranor human dose response curves and EC50s for various PPAR agonists

<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>

Lanifibranor binds differently than rosiglitazone to PPARγ inducing different coactivator recruitment(4)

Favorable safety profile differing from previously developed PPARs

<table>
<thead>
<tr>
<th>Organ</th>
<th>PPAR isoforms activated</th>
<th>Reported PPAR liabilities</th>
<th>Lanifibranor effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart</td>
<td>PPARγ</td>
<td>Fluid retention</td>
<td>Not observed</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cardiac hypertrophy</td>
<td></td>
</tr>
<tr>
<td>Skeletal muscle</td>
<td>PPARα</td>
<td>Myofiber degeneration</td>
<td>Not observed</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kidney</td>
<td>PPARα</td>
<td>&gt; 50% increases in creatinine, degenerative changes in renal tubules</td>
<td>Not observed</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urinary bladder</td>
<td>PPARγ</td>
<td>Proliferative changes in bladder epithelium</td>
<td>Not observed</td>
</tr>
</tbody>
</table>

**Plasma volume and heart weight after administration of PPAR agonists**

Source: Company data

Lanifibranor not associated with plasma volume expansion or heart weight increase

Source: Company data
Phase I and Phase IIa clinical studies\(^{(1)}\) demonstrated beneficial effects on key metabolic markers

**Lanifibranor metabolic markers in type II diabetic patients**

- Insulin resistance (HOMA-IR, adiponectin)
- Dyslipidemia (increase in HDL-C, reduction of TG)

**Clinical findings underline the favorable tolerability of lanifibranor**

- Good overall tolerance and no major safety findings
- No increases of creatinine, LFTs, or CPK
- No changes in blood pressure
- No signal of fluid overload or hemodilution
- No clinically relevant weight gain

Source: Company data and * Ohashi, Endocr Metab Immune Disord Drug Targets. 2015. Note: (1) Conducted by Abbott
Systemic sclerosis overview

A severe orphan disease with no approved treatment (1)

- SSc is a rare autoimmune rheumatic disease characterised by microvascular damage and progressive fibrosis of the skin and visceral organs
- There are two principal forms:
  - Limited cutaneous (lcSSc; ~60% of patients): restricted skin involvement and delayed onset organ involvement
  - Diffuse cutaneous (dcSSc; ~ 35% of patients): extensive skin and rapid onset organ involvement
  - SSc sine scleroderma: infrequent variation of the disease representing remaining 5%
- Current treatments include: immunosuppressant agents, corticosteroids at low-dose, or specific therapies targeting symptoms (endothelin-receptor antagonists to treat digital ulcers, ACE inhibitors to treat renal crisis, ...), HSCT
- High cost burden to society with patients affected by significantly impaired quality of life and shorter life expectancy
- Modified Rodnan Skin Score (MRSS): clinically validated and FDA/EMA-accepted as an end-point for marketing approval
- Potential for conditional approval

Prevalence: 154 per million in each of U.S. and Europe

<table>
<thead>
<tr>
<th>USA</th>
<th>Europe Top 5</th>
<th>Japan</th>
</tr>
</thead>
<tbody>
<tr>
<td>~102,000 patients(2)</td>
<td>~67,000 patients(2)</td>
<td>~4,800 patients(2)</td>
</tr>
</tbody>
</table>

Mortality rate is greater than in any other rheumatic disease(3)

Source: (1) Eular SSc Trials and Research Group, EUSTAR, SSc Research Foundation, Canadian SSc research group ; (2) Venture Valuation 2015; estimated figures for 2021 (3) ACR 2017 SSc Disease education
SSc pathogenesis and PPAR clinical rationale

SSc pathogenesis

Inflammation

The immune system produces cytokines leading to inflammation

Fibrosis

Overproduction of collagen leading to skin and vital organs fibrosis and failure (lung, kidney, heart)

Blood vessel damage and vascular remodelling

Reduction in blood flow to tissues causing damage

Lanifibranor rationale

PPARα, δ and γ have broad anti-inflammatory properties

PPARγ has anti-fibrotic properties in multiple organs

PPARδ and γ activation prevents vascular remodeling and positively impacts pulmonary arterial hypertension (PAH)
Pre-clinical studies show that lanifibranor inhibits TGFβ signaling in fibroblasts from SSc patients

Fibroblast to myofibroblast differentiation drives fibrosis across multiple organs and tissues and is largely regulated by TGF-β through the SMAD2/3 pathway

Lanifibranor blocks pSMAD2/3 accumulation in the nucleus, the differentiation of fibroblasts into myofibroblasts (α-SMA) and the expression of the collagen gene

Lanifibranor has demonstrated anti-fibrotic activity in multiple models and several organs that are relevant to SSc

Lanifibranor positively impacts the most relevant clinical features of SSc

### Lanifibranor effect on skin fibrosis

![Graph showing hydroxyproline levels](image)

### Lanifibranor effect on kidney fibrosis

![Graph showing collagen levels](image)

### Lanifibranor effect on lung fibrosis

![Graph showing collagen levels](image)

### Lanifibranor effect on lung functional capacity

![Graph showing FRC/Tidal volume](image)

Lanifibranor positively impacts vascular remodeling in the Fra2 model

### Lanifibranor effect on RVSP

![Graph showing RVSP](image)

### Lanifibranor effect on Fulton index

![Graph showing Fulton index](image)

### Lanifibranor effect on vessel wall thickness

![Graph showing wall thickness](image)

### Lanifibranor effect on vessel muscularization

![Graph showing vessel muscularization](image)

Source: Company data and Ruzehaji N. et al., Ann. Rheum. Disease 2016; ; (1) RVSP: Right Ventricular Systolic Pressure

Corporate Presentation | 2019

Non-confidential – Property of Inventiva
FASST Phase IIb trial in SSc

Trial design

Principal investigator

- Principal investigators: Prof. Allanore (Hôpital Cochin, Paris) and Prof. Denton (University College of London )
- Other: Prof. Matucci (Florence University, Italy), Prof. Distler (University of Erlangen, Germany), Prof. Distler (Universitaet Zurich, Switzerland)
- US scientific advisors: Prof. John Varga (Northwestern University), Prof. Dinesh Khanna (Michigan University)

Status

- Last patient recruited in October 2017
- Last patient last visit: October 12th 2018
- Three DSMB reviews (last one early July 2018) which recommended to continue the study unchanged

Results expected in Q1 2019

- Explore possibility of conditional marketing approval with EMA in H2 2019

Inclusion criteria

- MRSS (Modified Rodnan Skin Score) between 10 and 25
- SSc diagnosed less than 3 years ago

Primary endpoint

- Mean change of the MRSS from baseline

Key secondary endpoints

- MRSS responder rate, change from baseline in FVC%, digital ulcers, severe organ involvement, safety

Clinicaltrials.gov identifier: NCT02503644

145 patients

48 week treatment

Double blind randomized placebo controlled

Placebo, ~48 patients

Lanifibranor, 400 mg bid, ~48 patients

Lanifibranor, 600 mg bid, ~48 patients

Follow up

4 weeks
Lanifibranor: potentially differentiated vs. other programs in development for SSc

<table>
<thead>
<tr>
<th></th>
<th>Lanifibranor</th>
<th>Tocilizumab</th>
<th>Nintedanib</th>
<th>Riociguat</th>
<th>Lenabasum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anti-fibrotic</td>
<td>✓</td>
<td>✗</td>
<td>✓</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>Anti-inflammatory activity</td>
<td>✓</td>
<td>✗</td>
<td>✗</td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>Skin effect</td>
<td>✓</td>
<td>✗</td>
<td>✓</td>
<td>✗</td>
<td>✓</td>
</tr>
<tr>
<td>Lung effect</td>
<td>✓</td>
<td>✓</td>
<td></td>
<td>✓</td>
<td>✗</td>
</tr>
</tbody>
</table>

October 2018 update: following negative Phase III, project stopped in SSc by Roche
NASH overview

A severe disease with no currently approved treatment

Healthy Liver → NAFLD → NASH → NASH with fibrosis → Cirrhosis

- 15-20% reversible
- 40-50% Severe liver damage

Cirrhosis → Hepato-carcinoma 2-3% per year → Death 30-40%

Liver transplant

The overall NASH prevalence in the adult population of the United States is believed to be approximately 12%

Lanifibranor’s mechanism of action addresses all the key features of NASH

**Metabolism**
- **PPARα,δ,γ**
  - Insulin sensitivity
  - HDLc
  - TG

**Steatosis**
- **PPARα,γ**
  - FA uptake
  - FA catabolism
  - Lipogenesis

**Inflammation and Ballooning**
- **PPARα,δ,γ**
  - NFκB-dependent gene activation
  - Inflammasome
  - Ballooning

**Fibrosis**
- **PPARγ**
  - Stellate cell proliferation and activation
  - Collagen and fibronectin production
pan-PPAR clinical rationale in NASH (I)

- **PPARγ** activation by pioglitazone significantly improves steatosis, ballooning and inflammation as well as metabolic markers in NASH patients after 6 months or 18 months of treatment:

<table>
<thead>
<tr>
<th>Pioglitazone</th>
<th>6 mo (Belfort et al, 2006)</th>
<th>18 mo (Cusi et al, 2016)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Steatosis (% patients improved)</td>
<td>65% vs 38%, p &lt; 0.001</td>
<td>71% vs 26%, p &lt; 0.001</td>
</tr>
<tr>
<td>Inflammation (% patients improved)</td>
<td>65% vs 29%, p &lt; 0.001</td>
<td>49% vs 22%, p &lt; 0.001</td>
</tr>
<tr>
<td>Ballooning (% patients improved)</td>
<td>54% vs 24%, p &lt; 0.001</td>
<td>51% vs 24%, p &lt; 0.001</td>
</tr>
<tr>
<td>NASH resolution (% patients)</td>
<td>NA</td>
<td>51% vs 19%, p &lt; 0.001</td>
</tr>
<tr>
<td>Fibrosis (mean change in score)</td>
<td>NS</td>
<td>- 0.5, p = 0.039</td>
</tr>
</tbody>
</table>

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
Pan-PPAR clinical rationale in NASH (II)

- **PPARα/δ** activation by elafibranor leads to significant improvement of ballooning and inflammation as well as metabolic markers in NASH patients after 12 months of treatment\(^1\):
  - NASH resolution in ITT: 19% vs 12%, \(p = 0.045\)
  - Steatosis in patients with bNAS>4 (% patients improved): 35% vs 18%, NS
  - Inflammation in patients with bNAS>4 (% patients improved): 55% vs 33%, \(p < 0.05\)
  - Ballooning in patients with bNAS>4 (% patients improved): 45% vs 23%, \(p = 0.02\)

- Patients with resolved NASH showed significant reduction in liver fibrosis while non-responders did not show any change from baseline

Source: Ratziu V, et al. Gastroenterology 2016. Note: (1) GOLDEN 505 study conducted by Genfit
Lanifibranor significantly reduces steatosis, inflammation, ballooning and fibrosis in preclinical models

Lanifibranor inhibits steatosis and inflammation in the MCD model

**Steatosis**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Average number of lipid droplets/HPF</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vehicle</td>
<td>300 ± 20</td>
</tr>
<tr>
<td>Lanifibranor 10 mg/kg</td>
<td>200 ± 10</td>
</tr>
<tr>
<td>Lanifibranor 30 mg/kg</td>
<td>100 ± 5</td>
</tr>
</tbody>
</table>

*** p < 0.001 compared to Vehicle

Lanifibranor significantly reduces ballooning and the NAS score in the foz/foz model

**Ballooning**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Ballooning score</th>
</tr>
</thead>
<tbody>
<tr>
<td>HFD</td>
<td>2.0 ± 0.5</td>
</tr>
<tr>
<td>HFD + Lanifibranor 10 mg/kg</td>
<td>1.5 ± 0.1</td>
</tr>
<tr>
<td>HFD + Lanifibranor 30 mg/kg</td>
<td>1.0 ± 0.0</td>
</tr>
<tr>
<td>ND (Normal Diet)</td>
<td>0.5 ± 0.0</td>
</tr>
</tbody>
</table>

*** p < 0.001 compared to HFD

Lanifibranor reverses established liver fibrosis in CCL4 models

**NAS Score**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>NAS Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>HFD</td>
<td>10 ± 2</td>
</tr>
<tr>
<td>HFD + Lanifibranor 10 mg/kg</td>
<td>8 ± 1</td>
</tr>
<tr>
<td>HFD + Lanifibranor 30 mg/kg</td>
<td>6 ± 1</td>
</tr>
<tr>
<td>ND (Normal Diet)</td>
<td>2 ± 0</td>
</tr>
</tbody>
</table>

*** p < 0.001 compared to HFD

Lanifibranor associated with beneficial effects on all NASH-relevant liver features

Source: Company data; The new-generation Pan-Peroxisome Proliferator-Activated Receptor Agonist IVA337 Protects the Liver From Metabolic Disorders and Fibrosis; Hepatology Communications, June 2017
Overview of NATIVE trial design

Trial design

Principal investigator
- Prof. Francque (Universitair Ziekenhuis, Antwerpen, Belgium)

Status
- Trial enrolling
- Results expected first-half 2020

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

Inclusion criteria
- Liver biopsy
- Moderate to severe patients with an inflammation and ballooning score of 3 or 4
- Steatosis score ≥ 1 and fibrosis score < 4 (no cirrhosis)

Primary endpoint
- Decrease from baseline ≥ 2 points of the inflammation and ballooning score without worsening of fibrosis
- Central reading for pre- (before randomization) and post-treatment biopsy

Clinicaltrials.gov identifier: NCT03008070

Screening
- Liver biopsy

End of treatment
- Liver biopsy

225 patients
24 week treatment
Double blind randomized placebo controlled

Placebo, 75 patients
Lanifibranor, 800 mg once daily, 75 patients
Lanifibranor, 1200 mg once daily, 75 patients

More information on: http://www.native-trial.com/
The NATIVE Phase IIb trial of lanifibranor in NASH

16 countries worldwide
- 13 in EU
- Canada
- Australia
- Mauritius

Principal investigator: Prof. Sven Francque, Belgium

Selection of U.S. sites ongoing

16 countries approved

75 sites involved
- 71 sites activated
- 60 sites screening

November 27th, 2018 status: 464 patients screened, 116 patients randomized
- 2 positive DSMB reviews
- Results expected first-half 2020
Update on US investigator-initiated Phase II trial in T2DM patients with NAFLD

**Trial design**

**Principal investigator**
- Prof. Kenneth Cusi (University of Florida)

**Randomisation**
- Randomized (1:1), double-blind, placebo-controlled
- Non-obese subject control group for the metabolic and imaging procedures
- N=64 calculated assuming a 35% relative reduction of IHGT\(^1\)

**Status**
- IND approved
- First Patient First Visit: August 2018
- Results expected first-half of 2020

**Primary endpoint**
- Change from baseline to week 24 in IHTG

**Key secondary endpoints**
- Proportion of responders (IHTG, NAFLD resolution)
- Change in hepatic fibrosis (MRE\(^2\), biomarkers)
- Change in metabolic outcomes (insulin sensitivity, DNL\(^3\), glycemic control, lipids)
- Safety

Clinicaltrials.gov identifier: NCT03459079

64 patients
24 week treatment
*Double blind randomized placebo controlled*

Healthy non-obese control group, 10 subjects
Placebo, 32 patients
Lanifibranor, 800 mg once daily, 32 patients

A positive study result would further reinforce lanifibranor’s profile in NAFLD and NASH patients with type 2 diabetes

---

\(^1\) Intrahepatic triglycerides \(^2\) Magnetic resonance elastography \(^3\) De-novo lipogenesis
Inventiva created panNASH™, a committee of international independent experts aiming to play an active role in developing and disseminating their NASH expertise among the scientific community, patients and other key stakeholders within the healthcare system. The committee includes European and American medical experts in areas related to NASH such as hepatology, diabetes and cardiology, along with renowned scientific experts focused on promoting a better understanding of the physiopathological mechanisms involved in NASH.

<table>
<thead>
<tr>
<th>Specialty</th>
<th>Country</th>
<th>Member</th>
<th>Affiliation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hepatology</td>
<td>Belgium</td>
<td>Prof. Sven Francque</td>
<td>Antwerp University Hospital</td>
</tr>
<tr>
<td>Hepatology</td>
<td>Germany</td>
<td>Prof. Frank Tacke</td>
<td>University Hospital Aachen</td>
</tr>
<tr>
<td>Hepatology</td>
<td>Switzerland</td>
<td>Prof. Jean-François Dufour</td>
<td>University Clinic Bern</td>
</tr>
<tr>
<td>Hepatology</td>
<td>United States</td>
<td>Prof. Manal Abdelmalek</td>
<td>Duke University</td>
</tr>
<tr>
<td>Hepatology</td>
<td>United States</td>
<td>Prof. Gyongyi Szabo</td>
<td>University of Massachusetts</td>
</tr>
<tr>
<td>Diabetology</td>
<td>Germany</td>
<td>Prof. Michael Roden</td>
<td>Heinrich Heine University</td>
</tr>
<tr>
<td>Diabetology</td>
<td>United States</td>
<td>Prof. Kenneth Cusi</td>
<td>University of Florida</td>
</tr>
<tr>
<td>Cardiology</td>
<td>UK</td>
<td>Prof. Christopher Byrne</td>
<td>University of Southampton</td>
</tr>
<tr>
<td>Cardiology</td>
<td>United States</td>
<td>Prof. Frank Sacks</td>
<td>Harvard T.H. Chan School of Public Health</td>
</tr>
</tbody>
</table>
**Lanifibranor: differentiated potential to address all features of NASH in safe and efficacious manner**

<table>
<thead>
<tr>
<th>Feature</th>
<th>Lanifibranor</th>
<th>Ocaliva</th>
<th>Elafibranor</th>
<th>Cenicriviroc</th>
<th>Selonsertib</th>
</tr>
</thead>
<tbody>
<tr>
<td>Metabolism</td>
<td>✔</td>
<td>✗</td>
<td>✔</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>Steato-hepatitis</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>Necro-inflammation</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>Fibrosis</td>
<td>✗</td>
<td>✔</td>
<td>Unclear</td>
<td>✔</td>
<td>✔</td>
</tr>
</tbody>
</table>
Lanifibranor: overall anticipated development plan

Phase IIb

- **2015**
  - H2

- **2016**
  - H1 | H2

- **2017**
  - H1 | H2

- **2018**
  - H1 | H2

- **2019**
  - H1 | H2

- **2020**
  - H1 | H2

**Results**

- **FDA preIND**
- **FDA IND**

- **EMA feedback on conditional marketing authorisation eligibility**
- **FDA potential breakthrough therapy status**

- **Start of pivotal Phase III study (EU & US)**

**Systemic sclerosis**

**NASH**

**NAFLD**

**Toxicology**

- **52-week study**
- **Carcinogenicity studies**

Prof. Cusi study in TD2M patients with NAFLD

Phase II

Start of FASST, NATIVE and Prof. Cusi trials corresponds to first patient screened
Odiparcil – MPS
Mucopolysaccharidoses (MPS) are devastating diseases with high unmet medical need

MPS is a group of inherited lysosomal storage disorders

- Autosomal recessive disorders characterized by accumulation of glycosaminoglycan(s) (GAGs) due to deficient lysosomal enzymes
- Seven distinct clinical types based on the enzyme affected
- Odiparcil could be the first substrate reduction therapy for five forms of MPS with the following incidences:
  - MPS I: 1/100,000
  - MPS II: 1/100,000
  - MPS IV type A: 1/40,000 to 1/200,000
  - MPS VI: 1/240,000 to 1/400,000
  - MPS VII: very rare

MPS has devastating clinical consequences: example MPS I, II and VI

<table>
<thead>
<tr>
<th>Consequences</th>
<th>MPS I</th>
<th>MPS II</th>
<th>MPS VI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mental retardation</td>
<td>✔</td>
<td>✔</td>
<td></td>
</tr>
<tr>
<td>Coarse facies, short stature</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>Dysostosis multiplex</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>Joint stiffness</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>Spinal cord compression</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>Organomegaly</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>Poor vision (corneal clouding)</td>
<td>✔</td>
<td>✔(1)</td>
<td>✔</td>
</tr>
<tr>
<td>Hearing loss</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>Cardiac/respiratory disease</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>(1) Retinal degeneration with no corneal clouding</td>
<td>✔</td>
<td></td>
<td>✔</td>
</tr>
</tbody>
</table>

Source: (1) Source: Rheumatology 2011 Therapy for mucopolysaccharidoses; Vassili Valayannopoulos and Frits A. Wijburg
Enzyme replacement therapy (ERT) is commercially successful, but with limited therapeutic efficacy

Enzyme replacement therapies are standard of care in MPS

- Recombinant human enzymes, administered once a week as an intravenous infusion over 4 hours
- Approximately 50% of patients experience infusion reactions initially, some can be life threatening
- Limited penetration into protected or poorly vascularized tissues such as cornea or cartilage, where MPS symptoms often manifest

<table>
<thead>
<tr>
<th>Product</th>
<th>Company</th>
<th>MPS</th>
<th>Est. yearly cost</th>
<th>2017 sales</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aldurazyme</td>
<td>Genzyme</td>
<td>MPS I</td>
<td>$217K</td>
<td>$207M</td>
</tr>
<tr>
<td>Elaprase</td>
<td>Shire</td>
<td>MPS II</td>
<td>$522K</td>
<td>$616M</td>
</tr>
<tr>
<td>Vimizim</td>
<td>BiOMARIN</td>
<td>MPS IVA</td>
<td>$578K</td>
<td>$413M</td>
</tr>
<tr>
<td>Naglazyme</td>
<td>BiOMARIN</td>
<td>MPS VI</td>
<td>$476K</td>
<td>$332M</td>
</tr>
<tr>
<td>Mepsevii</td>
<td>Ultragenyx</td>
<td>MPS VII</td>
<td>$550K</td>
<td>n/a, approved Nov 2017</td>
</tr>
</tbody>
</table>

Source: Sales - Company annual reports 2017; WAC without discounts for a 25-kg patient - BioCentury "Making of MEPSEVII" Dec 11, 2017

ERT is expensive and usually requires outpatient administration. Significant unmet need remains in addressing symptoms in organs where ERT fails to penetrate

Source: (1) H. Noh, J. I. Lee; Current and potential therapeutic strategies for mucopolysaccharidoses; Journal of Clinical Pharmacy
# Odiparcil: an orally available small molecule substrate reduction therapy to treat several forms of MPS

<table>
<thead>
<tr>
<th>Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>▶ Decreases lysosomal accumulation of GAGs by <strong>modifying how DS and CS are synthesised</strong> – promotes formation of soluble DS / CS which can be excreted in the urine, rather than accumulating in cells</td>
</tr>
<tr>
<td>▶ <strong>Oral administration</strong></td>
</tr>
<tr>
<td>▶ <strong>Wide distribution</strong> in tissues that are poorly penetrated by enzyme replacement therapy</td>
</tr>
<tr>
<td>▶ Odiparcil-mediated reduction of intracellular GAG accumulation <strong>demonstrated in <em>in vitro</em> and <em>in vivo</em> models</strong></td>
</tr>
<tr>
<td>▶ US biomarker study finalized and Phase IIa study in MPS VI initiated - <strong>data expected H2 2019</strong></td>
</tr>
<tr>
<td>▶ Potential to be prescribed in <strong>combination with ERT and also as potential monotherapy</strong></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Safety</th>
</tr>
</thead>
<tbody>
<tr>
<td>▶ <strong>Low toxicity in vivo</strong></td>
</tr>
<tr>
<td>▶ <strong>Favorable safety and tolerability</strong> profile in multiple Phase I and Phase II clinical studies in unrelated indication(1) (administered to &gt;1,800 subjects) allowing the commencement of a POC study in MPS VI patients</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>IP</th>
</tr>
</thead>
<tbody>
<tr>
<td>▶ Method of use patent filed in 2013 and granted in EU (Nov. 2015) and the US (Feb. 2017): <strong>LOE(2) 2039</strong> including 5-year extension</td>
</tr>
<tr>
<td>▶ MPS VI <strong>Orphan Drug Designation</strong> granted in the US and in the EU</td>
</tr>
</tbody>
</table>

---

(1) Trial conducted by GSK prior to Inventiva’s founding (2) LOE: Loss of exclusivity
Unique mechanism of action potentially synergistic with ERT

Odiparcil diverts endogenous protein-bound GAG synthesis to soluble odiparcil-bound chondroitin sulfate (CS) and dermatan sulfate (DS) synthesis

Odiparcil decreases intracellular GAG accumulation \textit{in vitro} in MPS VI patient cells

Odiparcil observed to reduce GAG accumulation in MPS VI patient cells

\textbf{Source:} H. Noh, J. I. Lee; Current and potential therapeutic strategies for mucopolysaccharidoses; Journal of Clinical Pharmacy, company data
By producing soluble dermatan and chondroitin sulfates, odiparcil can address several types of MPS

<table>
<thead>
<tr>
<th>Type</th>
<th>Name</th>
<th>Deficient Lysosomal Enzyme</th>
<th>Incidence</th>
<th>Key Disease Features</th>
<th>DS</th>
<th>CS</th>
<th>HS</th>
<th>KS</th>
</tr>
</thead>
<tbody>
<tr>
<td>MPS I-H</td>
<td>Hurler syndrome</td>
<td>Alpha-L-iduronidase</td>
<td>1/100,000</td>
<td>Corneal clouding, skeletal abnormalities, organ enlargement, heart disease, mental retardation, death in childhood</td>
<td>✓</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MPS I-S</td>
<td>Scheie syndrome</td>
<td>Alpha-L- iduronidase</td>
<td>1/100,000</td>
<td>Corneal clouding, stiff joints, heart disease</td>
<td></td>
<td>✓</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MPS I-H/S</td>
<td>Hurler-Scheie syndrome</td>
<td>Alpha-L- iduronidase</td>
<td>1/100,000</td>
<td>Intermediate between MPS I-H and MPS I-S</td>
<td>✓</td>
<td></td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>MPS II</td>
<td>Types A &amp; B</td>
<td>Iduronate sulphatase</td>
<td>1/100,000</td>
<td>Corneal clouding, skeletal abnormalities, organ enlargement, heart disease, mental retardation (type B), death in childhood (type B)</td>
<td>✓</td>
<td></td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>MPS III</td>
<td>Sanfilippo syndrome</td>
<td>Heparan N-sulphatase; alpha-N-acetylg glucosaminidase; Acetyl-CoA and alpha-glucosaminide acyltransferase; N-acetylg glucosamine-6-sulphatase</td>
<td>1/25,000 to 75,000</td>
<td>Profound mental deterioration, hyperactivity and mild somatic manifestations</td>
<td></td>
<td></td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>MPS IV</td>
<td>Morquio syndrome</td>
<td>Galactose 6-sulphatase</td>
<td>1/40,000 to 200,000</td>
<td>Skeletal abnormalities, loose ligaments, degenerative joint disease, corneal clouding, heart disease, death in childhood or young adulthood</td>
<td>✓</td>
<td>✓</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MPS IV</td>
<td>Morquio syndrome</td>
<td>Beta- galactosidase</td>
<td>1/40,000 to 200,000</td>
<td>Similar to MPS IV Type A</td>
<td></td>
<td></td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>MPS VI</td>
<td>Maroteaux-Lamy syndrome</td>
<td>Arylsulphatase B</td>
<td>1/240,000 to 400,000</td>
<td>Similar to MPS I (excluding mental retardation), death in childhood or young adulthood</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>MPS VII</td>
<td>Sly syndrome</td>
<td>Beta- Glucuronidase</td>
<td>Very rare</td>
<td>Similar to MPS I</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
<td></td>
</tr>
</tbody>
</table>

Source: Rheumatology 2011 Therapy for mucopolysaccharides; Vassili Valayannopoulos and Frits A. Wijburg
Odiparcil decreases GAG content *in vivo* and improves mobility in a MPS VI model

*The doses administered provide exposure levels similar to that to be used in clinic*

**Wild-type and MPS VI mice**

- Treatment starts when animals are one month old

**6 months**

- Sulfated GAGs in organs/tissues and urine
- Mobility test
- Corneal structure/clouding

- **Odiparcil**
  - Given in food

---

**Odiparcil decreases GAG accumulation in tissues**

<table>
<thead>
<tr>
<th></th>
<th>Liver</th>
</tr>
</thead>
<tbody>
<tr>
<td>WT</td>
<td></td>
</tr>
<tr>
<td>MPS VI</td>
<td></td>
</tr>
<tr>
<td>MPS VI + Odi</td>
<td>-100%</td>
</tr>
</tbody>
</table>

*Chow diet  Odiparcil: 4.5 g/kg in food*

**Odiparcil decreases intra-cellular GAG**

<table>
<thead>
<tr>
<th>GAG Granules:</th>
<th>0</th>
<th>1-10</th>
<th>&gt;10</th>
</tr>
</thead>
<tbody>
<tr>
<td>WT</td>
<td>40.4</td>
<td>45.8</td>
<td>9.4</td>
</tr>
<tr>
<td>MPS VI</td>
<td>15.1</td>
<td>32.6</td>
<td>51.3</td>
</tr>
<tr>
<td>MPS VI + Odi</td>
<td>19.7</td>
<td>47.4</td>
<td>21.5</td>
</tr>
</tbody>
</table>

*Chow diet  Odiparcil: 4.5 g/kg in food*

<table>
<thead>
<tr>
<th></th>
<th>time on pole [sec]</th>
</tr>
</thead>
<tbody>
<tr>
<td>WT</td>
<td></td>
</tr>
<tr>
<td>MPS VI</td>
<td></td>
</tr>
<tr>
<td>MPS VI + Odi</td>
<td></td>
</tr>
</tbody>
</table>

*p<0.001  p<0.05*

**In vivo in MPS VI affected mice**

- Odiparcil decreases GAG accumulation in various tissues and intracellular GAG accumulation in lymphocytes
- Odiparcil decreases GAG accumulation in cornea, restores corneal structure and decreases GAG accumulation in cartilage
- Odiparcil restores mobility

Source: Company data
Visual impairment and cartilage-linked manifestations in MPS VI are a major medical unmet need

**Cornea – impaired vision**
- Visual impairment affects many MPS VI patients
- Preservation of vision is important as lifespan and other morbidities improve

Corneal opacification is a major driver of visual acuity decrease
- Diffuse, ‘ground-glass’ corneal opacification
- Slowly progressive but may be present from infancy

Pathophysiology of corneal clouding
- Corneal clarity depends on regular arrangement of collagen fibrils in corneal stroma
- Intracellular and extracellular deposition of GAGs in corneal stroma leads to the disruption of collagen spacing, size and arrangement and results in corneal clouding

Galsulfase does not penetrate the eye, does not address corneal opacification and subsequent ocular manifestations

**Cartilage – impaired mobility**
- GAGs accumulate in cartilages of MPS VI patients leading to cartilage thickening
  - Tracheal stenosis and/or tracheomalacia could lead to airway obstruction
  - Articular joint thickening leads to reduction of range of motion, pain, and poor quality of life
  - GAG accumulation in cardiac valves leads to dysmorphic and poorly mobile leaflets and subsequent valvular disease (regurgitation) requiring valve replacement (90% of MPS VI patients are affected)

Galsulfase does not efficiently penetrate the cartilage and does not address cartilage-linked manifestations

Galsulfase does not efficiently penetrate the cartilage and does not address cartilage-linked manifestations

**Source:** Design, baseline characteristics, and early findings of the MPS VI (mucopolysaccharidosis VI) Clinical Surveillance Program (CSP); Journal of Inherited Metabolism Disorders (2013)

**Slowing or halting progression or decreasing GAG accumulation in these organs would represent a major contribution to patient care**
Unlike ERT, odiparcil is a small molecule that we have observed to be well distributed in the body, even in tissues that are poorly vascularized or protected by a barrier.

While pre-clinical studies have observed the presence of rhASB in well-vascularized tissue in cat models, such as the heart muscle, they did not observe the presence of rhASB in the cornea or cartilage.

In pre-clinical studies in rodent models, we observed meaningful concentrations of odiparcil in not only heart muscle tissue, but also in tissues that are poorly vascularized or protected by a barrier: bone, corneal tissue and cartilage.

Source: (1) Odiparcil: tissue distribution following 25mg/kg oral administration, TID for 5 days; (2) Recombinant human ARB: Expressed as ratio of ARSB enzyme activity in the liver in MPS VI cats after repeat infusion (conditions: preliminary trial, Trial A and Trial B from Auclair et al. 2003)
Odiparcil impact on corneal GAG accumulation and corneal structure in MPS VI mice

Decreases in GAG accumulation and improvements in corneal structure expected to improve corneal function and ocular impairment

Source: Company data

Company: Inventiva
Odiparcil decreases GAG accumulation in cartilages in MPS VI mice

By decreasing GAG storage in cartilage, odiparcil improves cartilage-linked disease manifestations

Source: Company data
LeukoGAG biomarker for MPS VI demonstrates the incomplete impact of ERT and opportunity for odiparcil

- **Leukocytes are promising cells**: easy to collect; intracellular GAG levels are seen to be increased in animal model of MPS where odiparcil decreases intra-cellular GAG content

- **Objectives of Inventiva’s non-interventional study**: develop a robust quantification method to measure intracellular HS, CS and DS in leukocytes and an activity biomarker to be used in clinical trials

- **Population**: 6 MPS VI patients on ERT and 6 age matched control subjects not affected with MPS

- **Investigational site**: Dr. Paul Harmatz (PI), UCSF Benioff Children’s Hospital in Oakland (CA, USA)

### MPS VI patients treated with ERT have increased CS and DS levels in urine

<table>
<thead>
<tr>
<th>CS</th>
<th>DS</th>
</tr>
</thead>
<tbody>
<tr>
<td>7-15y</td>
<td>&gt;16y</td>
</tr>
</tbody>
</table>

### ARSB\(^{(1)}\) activity in leukocytes is increased by 8 fold after ERT infusion

### MPS VI patients treated with ERT have increased CS (and DS levels) in leukocytes

MPS VI patients treated with Naglazyme maintained a high level of intracellular DS and CS levels in leukocytes compared to age matched healthy volunteers suggesting the possibility to further reduce this level with odiparcil

(1) Arylsulfatase B, which is involved in the breakdown of GAGs
iMProveS Phase IIa trial of odiparcil in MPS VI

**Phase IIa**
- Phase 3 enabling study with evidence for dose selection and PK / PD response characterization
- Clinicaltrials.gov identifier: NCT03370653

**Population**
- Receiving ERT (N=18)
- Not receiving ERT (N=6)

18 patients **double blind** + 6 patients **open label**

26 week treatment

- Placebo + ERT, 6 patients
- Odiparcil, 250 mg bid + ERT, 6 patients
- Odiparcil, 500 mg bid + ERT, 6 patients
- Odiparcil, 500 mg bid, 6 patients ERT naive

**Endpoints**

**Safety**
- Clinical and biological assessments (standard tests)

**Pharmacokinetics**
- Odiparcil plasma levels

**Efficacy**
- Leukocyte, skin and urinary GAG content
- Activity and mobility tests (6 minute walk test, upper limb function, shoulder mobility range)
- Cardiac, vascular and respiratory functions
- Eye impairment, hearing capacity, pain assessment, quality of life questionnaires

**Status**
- Design discussed with EMA (2016)
- Recruiting
- EU, multicenter: UK, Germany, France, Portugal
- Results expected second-half of 2019

Odiparcil has the potential to positively differentiate versus current MPS treatment options

<table>
<thead>
<tr>
<th></th>
<th>Odiparcil</th>
<th>Aldurazyme, Elaprase, Naglazyme, Vimizim, Mepsevii</th>
<th>HSCT (Hematopoietic stem cell transplantation)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Effect on mobility</td>
<td>✓</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Effect on eye, cartilage, bones, heart valves, spinal cord compression</td>
<td>✓</td>
<td>✗</td>
<td>✗</td>
</tr>
<tr>
<td>Distribution type</td>
<td>Oral</td>
<td>Intravenous Infusion</td>
<td>Transplantation</td>
</tr>
</tbody>
</table>

Source: Company evaluation
Odiparcil overall anticipated development plan in MPS VI

2016
H2

2017
H1 | H2

2018
H1 | H2

2019
H1 | H2

2020
H1 | H2

2021
H1 | H2

2022
H1

Clinic

Biomarker study

Phase lia (MPS VI adults)

SAFE-KIDDs

Phase I/II (MPS VI children)

Toxicology

Juvenile Tox

Carcinogenicity

Rare paediatric designation

FDA IND

Start of pivotal study

Note: Start of iMProves trial corresponds to first patient screened
R&D collaborations and Hippo pathway program update
Key validating collaborations with AbbVie and Boehringer Ingelheim

RORγ collaboration in inflammatory disease

- RORγ program addresses large markets currently dominated by biologics and could prove to be superior to biologics
- AbbVie has started Phase I study with ABBV-157
- With the initiation of Phase I with ABBV-157 and the discovery of a back-up to this lead candidate, the work of Inventiva’s team to discover new orally available ROR inverse agonists is completed
- Inventiva remains eligible to future milestone payments and sales royalties on all ROR molecules identified during the collaboration

ABBV-157: Phase I studies initiated

Fibrosis collaboration

- Multi-year R&D collaboration and licensing partnership
- Joint team until pre-CC stage. BI to take full responsibility of clinical development and commercialization
- Inventiva eligible to up to ~€170m in milestones plus royalties
- Following the validation of this new target supporting its therapeutic potential in fibrotic conditions, Boehringer Ingelheim exercised the option to jointly develop this target triggering a milestone payment of €2.5m
- The collaboration has entered into the screening phase and the first molecules identified are currently being optimized by the Inventiva and Boehringer-Ingelheim teams

Program progressing as planned with first screening performed
Hippo pathway: update on program progress

The Hippo pathway: an oncogenic signalling pathway implicated in oncogenic and fibrotic processes

- Targets the YAP/TEAD transcriptional complex
- The program has the potential to address both rare cancers (malignant mesothelioma, uveal melanoma) and prevalent cancers (NSCLC, TNBC, hepatoblastoma, hepatocellular carcinoma) as well as fibrotic diseases
- Molecules inhibiting the YAP/TEAD interaction have the potential to overcome drug resistance and tumor escape mechanisms
- Two non-dilutive grants secured and large academic network in place

Recently generated data

- *In vitro* data on transactivation and proliferation
- Data showing Inventiva’s molecule blocks YAP/TEAD target genes
- *In vivo* data in xenograft and PDX models with potential for efficacy as stand-alone treatment or in combination with standard of care
- Two molecules identified with properties allowing start of non-GLP tox
- Three patents filed directed toward covering one chemical family
- Back-up program ongoing and new molecules with optimized properties identified

The program is expected to enter into Phase I/II enabling preclinical development in 2019
Conclusions
### Recent achievements and upcoming expected milestones

<table>
<thead>
<tr>
<th>2018</th>
<th>2019</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Lanifibranor</strong></td>
<td></td>
</tr>
<tr>
<td>✔ 2 year carcinogenicity study results</td>
<td>▶ Pivotal Phase IIb SSc results - Q1 2019</td>
</tr>
<tr>
<td>✔ US fibrosis indication patent</td>
<td>▶ Last patient Phase IIb NASH</td>
</tr>
<tr>
<td>✔ US IND</td>
<td>▶ Last patient Prof. Cusi study in NAFLD patients with TD2M</td>
</tr>
<tr>
<td>✔ First patient in NAFLD Phase II</td>
<td></td>
</tr>
<tr>
<td><strong>Odpiparil</strong></td>
<td></td>
</tr>
<tr>
<td>✔ MPS VI biomarker study results</td>
<td>▶ Phase IIa MPS VI results - H2 2019</td>
</tr>
<tr>
<td>✔ Juvenile tox results</td>
<td>▶ Launch of Phase Ib in children - H1 2019</td>
</tr>
<tr>
<td><strong>Collab.</strong></td>
<td>▶ Rare pediatric disease designation MPS VI</td>
</tr>
<tr>
<td>✔ Start Phase I with ABBV-157</td>
<td></td>
</tr>
<tr>
<td><strong>Discovery</strong></td>
<td><strong>Finance</strong></td>
</tr>
<tr>
<td>✔ YAP/TEAD: <em>In vivo</em> POC</td>
<td>✔ Capital increase</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Contacts

Inventiva
Frédéric Cren
CEO
info@inventivapharma.com
+33 (0)3 80 44 75 00

Brunswick
Julien Trosdorf / Yannick Tetzlaff
Media relations
inventiva@brunswickgroup.com
+ 33 1 53 96 83 83

LifeSci Advisors
Monique Kosse
Investor relations
monique@lifesciaidvisors.com