PRESS RELEASE

Inventiva's lanifibranor meets the primary and key secondary endpoints in the Phase IIb NATIVE clinical trial in non-alcoholic steatohepatitis (NASH)

- Lanifibranor met the primary endpoint with a statistically significant reduction 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 populations (PP[2])
- Lanifibranor also met key secondary endpoints including NASH resolution with no worsening of fibrosis[3] and improvement of liver fibrosis with no worsening of NASH[4] in both ITT and PP populations
- Lanifibranor is the first drug candidate to achieve statistically significant effects on NASH resolution with no worsening of fibrosis and improvement of fibrosis with no worsening of NASH, the FDA and EMA primary endpoints relevant for seeking accelerated approval during future Phase III clinical development
- 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

Trial results to be presented during conference calls in French at 7:30 am CET and in English at 2:00 pm CET on June 16, 2020

Daix (France), June 15, 2020 – Inventiva (Euronext: IVA), a clinical-stage biopharmaceutical company developing oral small molecule therapies for the treatment of non-alcoholic steatohepatitis (NASH), mucopolysaccharidoses (MPS) and other diseases with significant unmet medical need, today announced positive topline results from the Phase IIb NATIVE (NAsh Trial to Validate IVA337 Efficacy) clinical trial evaluating lanifibranor for the treatment of NASH.

[1] ITT: includes all patients randomized in the trial.
[2] PP: includes all patients with paired biopsies and without deviation impacting efficacy assessment.
[3] *NASH resolution* and *no worsening of fibrosis* defined as CRN Lobular inflammation score equal to 0 or 1 and CRN Hepatocyte ballooning score equal to 0 and no worsening of the CRN-Fibrosis score.
[4] *Improvement of liver fibrosis with no worsening of NASH* defined as improvement of CRN-Fibrosis score $\geqslant$ 1 stage and no increase of CRN-Steatosis score and no increase of CRN-Inflammation score and no increase of CRN-Ballooning score.

In this 24-week clinical trial, lanifibranor, an orally-available small molecule and the only pan-PPAR agonist[5] currently in clinical development for the treatment of NASH, met the primary endpoint in the ITT population at the dose of 1200mg/day with a statistically significant (p = 0.004) decrease of at least two points in the SAF activity score[6] (combining hepatocellular inflammation and ballooning), compared to baseline, with no worsening of fibrosis. 49% of patients in the lanifibranor 1200mg/day dose group achieved the primary endpoint compared to 27% in the placebo arm.

Lanifibranor also met multiple key secondary endpoints including:

- Resolution of NASH with no worsening of fibrosis in both dose groups (800mg/day and 1200mg/day)
- Improvement of fibrosis by at least one stage[7] with no worsening of NASH at the 1200mg/day dose group
- NASH resolution and improvement of fibrosis in both dose groups (800mg/day and 1200mg/day)

Statistically significant results were also obtained in both dose groups (800mg/day and 1200mg/day) on:

- Decrease of insulin, fasting glucose and glycated haemoglobin (HB1AC) in patients with type 2 diabetes
- Decrease in triglycerides
- Increase in high density lipoprotein cholesterol (HDL)
- Decrease in liver enzymes (ALT, AST and GGT)

With these results, lanifibranor is the first drug candidate to achieve statistically significant results on the two Food and Drug Administration (FDA) and European Medicine Agency (EMA) primary endpoints[8] relevant for seeking accelerated approval during Phase III clinical development.

[5] A pan-PPAR agonist is a molecule designed to activate all three peroxisome proliferator-activated receptor (PPAR) isoforms (PPARα, PPARδ, PPARγ), which are well-characterized nuclear receptor proteins that regulate gene expression.

[6] Steatosis, Activity and Fibrosis score, which is a commonly accepted, semi-quantitative evluation of liver biopsy results.

[7] Improvement in hepatic fibrosis $\geqslant$ 1 stage with no increase in NASH at week 24: Improvement in CRN-F $\geqslant$ 1 stage with no increase in CRN-S, CRN-I or CRN-B

[8] NASH resolution with no worsening of fibrosis and improvement of fibrosis with no worsening of NASH.

		Primary and key secondary endpoints					
		Intention to Treat Population (ITT)			Per Protocol Population (PP)		
		Placebo (N = 81)	Lanifibranor		Placebo (N = 62)	Lanifibranor	
			800mg (N = 83)	1200mg (N = 83)		800mg (N = 63)	1200mg (N = 69)
Primary endpoint	Decrease of ≥2 points of SAF activity score[1]	27%	41% *P=0.061*	49% *P=0.004**	34%	51% *P=0.058*	55% *P=0.015**
Secondary endpoints	Resolution of NASH and no worsening of fibrosis[2]	19%	33% *P=0.043**	45% *P<0.001**	23%	40% *P=0.039**	49% *P=0.002**
	Resolution of NASH and no worsening of fibrosis[2] in F2/F3 patients[3]	9%	34% *P=0.011**	44% *P<0.001**	11%	40% *P=0.016**	51% *P<0.001**
	Improvement of fibrosis by at least one stage and no worsening of NASH [4]	24%	28% *P=0.53*	42% *P=0.011**	29%	32% *P=0.75*	46% *P=0.04**
	Resolution of NASH and improvement of fibrosis [5]	7%	21% *P=0.017**	31% *P<0.001**	10%	24% *P=0.036**	33% *P=0.001**
	Decrease of ≥ 2 points of NAS score [6] (NAFLD activity score) and no worsening of fibrosis	32%	52% *P=0.01**	64% *P<0.001**	40%	62% *P=0.02**	71% *P<0.001**

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

1. *Response is defined as a decrease from baseline to week 24 of at least 2 points of the SAF Activity score (SAF-A) with no worsening of the CRN Fibrosis score (CRN-F). No worsening means that score remains stable or decreases.*
2. *Resolution of NASH with no worsening of fibrosis at week 24: CRN-I = 0 or 1 (CRN-Inflammation), CRN-B = 0 (CRN-Ballooning) and no worsening of CRN-F from baseline.*
3. Includes 188 patients in the ITT population and 149 in the Per Protocol population.
4. *Improvement of liver fibrosis ≥ 1 stage and no worsening of NASH at week 24: Improvement of CRN-F ≥ 1 stage and no increase of CRN-S, CRN-I or CRN-B*
5. *Resolution of NASH and improvement of fibrosis at week 24: CRN-I = 0 or 1, CRN-B = 0 and an improvement of CRN-F ≥ 1 stage.*
6. NAS score is a commonly accepted, semi-quantitative evaluation of biopsy results that assesses the severity of steatosis, inflammation and ballooning in the liver.

Prof. Sven Francque, M.D., Ph.D. from Antwerp University Hospital and co-principal investigator of the Phase IIb NATIVE clinical trial, said: *"The topline results delivered by lanifibranor, the only pan-PPAR agonist currently in clinical development in NASH, are extremely encouraging, especially given the short treatment period of only six months. The results observed within such a short timeframe suggest that extended treatment could even lead to further improvements in liver health. Supported by these positive trial results in NASH resolution and fibrosis reduction, lanifibranor is positioned as a promising drug candidate in NASH and we look forward to its pivotal Phase III development."*

Prof. Manal Abdelmalek, M.D., M.P.H. from Duke University and co-principal investigator of the Phase IIb NATIVE clinical trial, added: *"These are very exciting results which compare very favourably with those of other*

oral molecules currently in development for NASH. Lanifibranor, to my knowledge, is the first drug candidate that has been able to achieve statistically significant results on both FDA and EMA regulatory endpoints relevant for accelerated approval – NASH resolution and improvement of fibrosis. I am extremely encouraged by the results and the rapid onset of action observed with lanifibranor, with statistically significant results achieved on both NASH resolution and improvement of fibrosis after only six months of treatment. With the many challenges surrounding drug development for the treatment of NASH, it is great to have lanifibranor achieve these positive results."

Pierre Broqua, CSO and cofounder of Inventiva, stated: *"First of all, I would like to extend my deepest thank you to patients, caregivers, investigators, advisors and our team for their continued confidence, relentless dedication and strong commitment throughout this trial. We are all thrilled by these topline results, especially since, there is no approved treatment in NASH to date despite very significant medical needs. During this trial, lanifibranor met both the trial's primary and key secondary endpoints, which we credit to its differentiated mechanism of action. Given this was a global trial where lanifibranor met both FDA and EMA regulatory endpoints in only six months of treatment, we are optimistic about the potential of our drug candidate in a Phase III pivotal clinical trial."*

Safety and tolerability

Lanifibranor showed an overall favorable tolerability profile, consistent with observations from previous clinical trials. There were three discontinuations due to adverse events (AE) in each group. The AEs were generally mild to moderate in severity. There were 13 serious adverse events (SAE), three in the placebo arm, three in the 800mg/day dose group and seven in the 1200mg/day dose group. After excluding biopsy-related SAE, there were three SAE in the placebo group, two in the 800mg/day dose group and four in the 1200mg/day dose group.

Consistent with known insulin sensitizing pharmacology, a modest mean weight increase from baseline of 2.4 kg (2.6%) at the 800mg/day dose and 2.7 kg (3.1%) at the 1200mg/day dose was observed. A total of 14 patients reported peripheral edema, two in the placebo group, five in the 800mg/day dose group and seven in the 1200mg/day dose group. All of them except one were of mild intensity. There were only two patients with treatment-related peripheral edema in each lanifibranor treatment arms. There was no treatment discontinuation due to edema.

Patients reporting treatment-emergent Serious AE (SAE) N (%)	**Placebo (N = 81)**	**Lanifibranor 800mg (N = 83)**	**Lanifibranor 1200mg (N = 83)**
Total	3 (3.7%)	3 (3.6%)	7 (8.4%)
Treatment-Emergent Serious AE linked to biopsy procedure:			
- Post-procedural haematoma/haemorrhage	-	1 (1.2%)	1 (1.2%)
- Post-procedural pain	-	-	1 (1.2%)
- Pneumobilia (post-procedural)	-	-	1 (1.2%)
Other Treatment-Emergent Serious AE:			
- Wrist fracture	1 (1.2%)	-	-
- Angina unstable	-	-	1 (1.2%)
- Cardiac failure	1 (1.2%)	-	-
- Gastroenteritis	-	-	1 (1.2%)
- Pyelonephritis	-	-	1 (1.2%)
- Pancreatitis	-	1 (1.2%)	-
- Undifferentiated connective tissue disease	-	1 (1.2%)	-
- Urticaria	1 (1.2%)	-	-
- Foot operation	-	-	1 (1.2%)

Next steps

Following today's publication of positive topline results, Inventiva has decided to move forward with the clinical development of lanifibranor for the treatment of NASH and enter into pivotal Phase III development. To this end, the Company plans to finalize the relevant trial design and meet with regulatory authorities (FDA and EMA). Inventiva plans to present the Phase IIb NATIVE clinical trial results at the upcoming Liver Meeting® of the AASLD (American Association for the Study of Liver Diseases), taking place from November 13 to November 16, 2020.

Conference calls and webcasts

A **conference call** in **French** will be held **tomorrow, June 16, 2020 at 7:30 am (CET).** To join the conference call, please use the code **4982708** after dialing one of the following numbers:

France: +33 (0) 1 70 70 07 81
Belgium: +32 (0) 2 793 3847
Germany: +49 (0) 69 2222 2625
Netherlands: +31 (0) 20 795 6614
Switzerland: +41 (0) 44 580 7145
United Kingdom: +44 (0) 2071 928 338
United States: +1 646-741-3167

The presentation accompanying this conference call will be available on Inventiva's website from 7:30 am (CET) onwards in the "Investors" – "Investor presentations" section and can be followed live at: https://edge.media-server.com/mmc/p/2p5otx68.

A **conference call** in **English** will be held **tomorrow, June 16, 2020 at 2:00 pm (CET).** To join the conference call, please use the code **4785925** after dialing one of the following numbers:

France: +33 (0) 1 70 70 07 81
Belgium: +32 (0) 2 793 3847
Germany: +49 (0) 69 2222 2625
Netherlands: +31 (0) 20 795 6614
Switzerland: +41 (0) 44 580 7145
United Kingdom: +44 (0) 2071 928 338
United States: +1 646-741-3167

The presentation accompanying this conference call will be available on Inventiva's website from 7:30 am (CET) onwards in the "Investors" – "Investor presentations" section and can be followed live at: https://edge.media-server.com/mmc/p/dicwzktp.

A replay of both conference calls and the presentation will be available on Inventiva's website after the events at: http://inventivapharma.com/investors/investor-presentations/.

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About lanifibranor

Lanifibranor, Inventiva's lead product candidate, is an orally-available small molecule that acts to induce anti-fibrotic, anti-inflammatory and beneficial vascular and metabolic changes in the body by activating all three peroxisome proliferator-activated receptor (PPAR) isoforms, which are well-characterized nuclear receptor

proteins that regulate gene expression. Lanifibranor is a PPAR agonist that is designed to target all three PPAR isoforms in a moderately potent manner, with a well-balanced activation of PPARα and PPARδ, and a partial activation of PPARγ. While there are other PPAR agonists that target only one or two PPAR isoforms for activation, lanifibranor is the only pan-PPAR agonist in clinical development. Inventiva believes that lanifibranor's moderate and balanced pan-PPAR binding profile contributes to the favorable tolerability profile that has been observed in clinical trials and pre-clinical studies to date.

About the NATIVE Phase IIb trial

The NATIVE (NAsh Trial to Validate IVA337 Efficacy) clinical trial is a 24-week randomized, double-blind, placebo-controlled Phase IIb clinical trial evaluating lanifibranor for the treatment of patients with NASH. The main purpose of the trial is to assess the efficacy of lanifibranor in improving liver inflammation and ballooning, the two histological markers included in the definition of the regulatory endpoint of NASH resolution. To be considered for inclusion, patients were required to have: a diagnosis of NASH confirmed by liver biopsy; a cumulative score of inflammation and ballooning (as measured using the SAF scoring system) of three or four out of four, indicating the presence of moderate to severe inflammation and ballooning; a steatosis score greater than or equal to one, indicating the presence of moderate to severe steatosis; and a fibrosis score less than four, indicating the absence of cirrhosis. The primary endpoint of the trial is a reduction in the combined inflammation and ballooning score of two points compared to baseline, with no worsening fibrosis, as measured by the SAF score. Secondary endpoints include NASH resolution, improvements in each of the steatosis, inflammation, ballooning and fibrosis scores from baseline as measured using the SAF score, improvements in various other fibrosis measures, improvements in several metabolic markers, improvements in steatosis, inflammation and ballooning as measured using the NAS score (NAFLD activity score), and safety.

The trial randomized 247 patients with NASH in 71 sites in Australia, Canada, Europe, Mauritius and the United States.

About Inventiva

Inventiva is a clinical-stage biopharmaceutical company focused on the development of oral small molecule therapies for the treatment of NASH, MPS and other diseases with significant unmet medical need.

Leveraging its expertise and experience in the domain of compounds targeting nuclear receptors, transcription factors and epigenetic modulation, Inventiva is currently advancing two clinical candidates, as well as a deep pipeline of earlier stage programs.

Lanifibranor, its lead product candidate, is being developed for the treatment of patients with NASH, a common and progressive chronic liver disease for which there are currently no approved therapies.

Inventiva is also developing odiparcil, a second clinical stage asset, for the treatment of patients with MPS, a group of rare genetic disorders. A Phase Ib/II clinical trial in children with MPS VI is currently under preparation following the release of positive results of the Phase IIa clinical trial in adult MPS VI patients at the end of 2019.

In parallel, Inventiva is in the process of selecting an oncology development candidate for its Hippo signalling pathway program. Furthermore, the Company has established a strategic collaboration with AbbVie in the area of autoimmune diseases. AbbVie has started the clinical development of ABBV-157, a drug candidate for the treatment of moderate to severe psoriasis resulting from its collaboration with Inventiva. This collaboration enables Inventiva to receive milestone payments upon the achievement of pre-clinical, clinical, regulatory and commercial milestones, in addition to royalties on any approved products resulting from the collaboration.

The Company has a scientific team of approximately 70 people with deep expertise in the fields of biology, medicinal and computational chemistry, pharmacokinetics and pharmacology, as well as in clinical development.

It also owns an extensive library of approximately 240,000 pharmacologically relevant molecules, approximately 60% of which are proprietary, as well as a wholly-owned research and development facility.

Inventiva is a public company listed on compartment C of the regulated market of Euronext Paris (Euronext: IVA – ISIN: FR0013233012). www.inventivapharma.com

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This press release contains forward-looking statements, forecasts and estimates with respect to Inventiva's clinical trials, clinical trial data releases, clinical development plans and anticipated future activities of Inventiva. Certain of these statements, forecasts and estimates can be recognized by the use of words such as, without limitation, "believes", "anticipates", "expects", "intends", "plans", "seeks", "estimates", "may", "will" and "continue" and similar expressions. Such statements are not historical facts but rather are statements of future expectations and other forward-looking statements that are based on management's beliefs. These statements reflect such views and assumptions prevailing as of the date of the statements and involve known and unknown risks and uncertainties that could cause future results, performance or future events to differ materially from those expressed or implied in such statements. Actual events are difficult to predict and may depend upon factors that are beyond Inventiva's control. There can be no guarantees with respect to pipeline product candidates that the clinical trial results will be available on their anticipated timeline, that future clinical trials will be initiated as anticipated, or that candidates will receive the necessary regulatory approvals. Therefore, actual results may turn out to be materially different from the anticipated future results, performance or achievements expressed or implied by such statements, forecasts and estimates. Given these uncertainties, no representations are made as to the accuracy or fairness of such forward-looking statements, forecasts and estimates. Furthermore, forward-looking statements, forecasts and estimates only speak as of the date of this press release. Readers are cautioned not to place undue reliance on any of these forward-looking statements.

Please refer to the Universal Reference Document filed with the Autorité des Marchés Financiers on February 7, 2020 under n° D.20-0038 for additional information in relation to such factors, risks and uncertainties.

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