Mithra Reports Full Year 2021 Financial Results

- **Landmark year with the worldwide launch of first estetrol-based product Estelle®, leading to a cash collection of two major out-licensing milestones for an amount of EUR 24 million and product sales of EUR 13.4 million.**
- **Still around EUR 290 million cash to be collected for Estelle® out-licensing and sales related milestones.**
- **Cash position at EUR 32.9 million end 2021, strengthened by post-year end flexible equity financing agreement contracted with Goldman Sachs International for EUR 100 million**
- **Positive top-line results from Donesta® Phase 3 Studies, allowing to move forward the extended Clinical Program and to further broaden the scope of Donesta® as a global alternative for millions of menopausal women**

Liege, Belgium, 08 March 2022 – 7:30 CET – Mithra (Euronext Brussels: MITRA), a company dedicated to Women's Health, today announces its financial results for the year ended 31 December 2021, prepared in accordance with IFRS.

Leon Van Rompay, CEO Mithra Women's Health, commented: "*2021 marks a historical turning point with the worldwide launch of our first product containing a brand-new oestrogen estetrol, featuring improved safety and efficacy. On the other hand we have received our first top line clinical phase III results of our Donesta®, which have confirmed the tremendous potential as an innovative hormone therapy to treat many symptoms of estrogen loss simultaneously or sequentially throughout the entire menopausal period. We look forward to advancing our clinical development, including the initiation of three additional studies aimed at broadening the scope and the value of Donesta® in line with our new business development strategy.*

From a financial perspective, the approval of Estelle, directly followed by its commercial launch in the United States, Canada and a dozen of European countries, has enabled us to more than double our revenues in 2021 compared to last year. We are confident that this innovation in the women's contraceptive market will continue to increase its market penetration in these territories and together with launches in new territories we are set for an exciting 2022. The recent equity transaction with Goldman Sachs has strengthened our financial structure."

Financial highlights

- **Revenues** at EUR 22.7 million compared to EUR 9.0 million in 2020, mainly driven by EUR 13.4 million **first product sales of Estelle®** in the US, Canada and Europe; and an out-licensing revenue of EUR 3.7 million following the acquisition of full global licensing and distribution rights for Zoreline® allowing a deferred revenue to be recognized.
- **Cash collection of two major Estelle® out-licensing milestones** with Mayne (USD 11 million) and Gedeon Richter (EUR 15 million), without impact on revenue as already recognized in 2019

as per IFRS15. **Still around EUR 290 million cash to be collected for Estelle®** out-licensing and sales related milestones.

- **R&D expenses** (excluding depreciation, as presented in the alternative performance measure) stand at EUR 76.6 million compared to EUR 69.3 million in 2020. These R&D expenses are the result of the ramp-up of activities under the Phase III Donesta®.
- **EBITDA** stands at EUR -77.5 million compared to EUR -73.8 million at 2020. The variance is mainly explained by operating expenses increase, notably R&D expenses, compensated by gross profit increase and other operating income decrease.
- **Below EBITDA**, a net fair value loss on financial assets of EUR -6.4 million has been recognized. This loss is mainly explained by a charge of EUR 8 million related to a contingent receivable with Ceres Pharma, partly compensated by a gain on contract assets (related to the Mayne US deal).
- **Reception of 85.8 million ordinary shares** (an Estelle® out-licensing milestones for the US territory) allowing the Company to become the first shareholder (with 9.57%) of **Mayne Pharma** Group Ltd, an Australia-listed company on ASX.
- **Complete buyout of all earnouts linked to Myring® and Zoreline®**, cancelling related amounts reported in the balance sheet in December 2020 (EUR 8.8 million) and thus facilitates Mithra's equity story. This deal also allowed the Company to increase the value of Zoreline® IP rights on our balance sheet by EUR 8.5 million.
- As contractually agreed, an **instalment of EUR 25 million** was paid to former owners of Uteron Pharma[1]. This payment contributed to further decrease the liability reported at fair value on the balance sheet (from EUR 115.7 million in December 2020 to EUR 110.0 million in December 2021).
- **EUR 32.9 million net cash position**, on the top of which the **following facilities** are available :
    - EUR 100 million flexible equity financing agreement contracted with Goldman Sachs International in February 2022 with a first drawing request exercised on 4 February 2022 for an amount of EUR 10 million;
    - EUR 41 million as per December 31, 2021 in the framework of LDA capital commitment agreement (the Company has agreed with Goldman Sachs during any drawing period to not issue any put option notice under the LDA capital facility). Following the put option issued on 20 December 2021, a capital increase for an amount of EUR 8.1 million was completed on 14 February 2022 leading to an amount available under the LDA capital commitment of around EUR 33 million.
- **New credit line concluded for an amount of EUR 15 million.** This additional financing facility and the previously contracted credit line (EUR 20 million) are fully drown as per year end.
- **Equity stands at EUR 33.8 million**, reduced compared to December 2020 (EUR 157.7 million) by the total comprehensive loss for the period (EUR 134.2 million), partially compensated by two capital increases for a total amount of EUR 9.2 million (LDA capital and exercise of subscription rights).

[1] Mithra's press release, 01/10/2019

Operational Highlights (including post-period end)

Estetrol (E4) Platform

- **Landmark milestone for the Company** with **marketing authorizations for Estelle®** obtained in Canada (March), United States (April), Europe (May), Russia (September) and Australia (November).
- **Commercial launch of Estelle®** in the United States by Mayne Pharma (June) and in Canada by Searchlight Pharma (August) under the trademark Nextstellis®. Covid-19 impact (e.g., reduced physician visits on both the patient and medical representative side, material absences in our partner teams,…) and unrestricted coverage access challenges has slowed down product uptake. Nevertheless, current metrics show consistently that product market launch should gain momentum in 2022.
- **Gradual launch of Estelle® in Europe** by Gedeon Richter under the trademark Drovelis® in Austria, Germany, France, Luxemburg, Hungary, Italy, Slovakia, Poland, Czech Republic, Portugal and Belgium (also commercialized by Ceres Pharma under the trademark Lydisilka®). Current launch data shows Estelle® is within the launch trajectory of recent contraceptives launched despite Covid-19 impact (reduced physician visits).
- **Positive efficacy top-line results from Donesta® Phase 3** clinical trials for the treatment of vasomotor symptoms in post-menopausal women. Donesta® demonstrated a meaningful reduction in vasomotor symptoms from baseline and compared to placebo. All co-primary efficacy endpoints were statistically (all $p<0.01$) met in C301 (Europe, Latam and Russia) and in C302 (North America) studies, except for a borderline non-significant result for the severity criteria at week 4 in the C302 study, which reached and exceeded statistical significance by week 5 ($p<0.01$). Both studies also showed that the number and severity of hot flushes continued to decrease week after week until the end of the study, i. e. 3 months of treatment. Secondary endpoints evaluated at 3 months in the C301 study suggest a very positive impact of Donesta® on the quality of life.
- **Extension of the Donesta® Clinical Program with three new studies** carried out on estetrol's effect on symptoms significantly impacting postmenopausal women's quality of life: vulvovaginal atrophy, skin health and hair quality. Depending on the feedback of the regulatory authorities, Mithra expects to start these clinical trials in 2022.
- Based on regulatory agencies' feedback, the Board of Directors decided in September 2021 that the initial **PeriNesta® development project** was no longer timely nor a priority for the Company.
- **Topline results of the Coronesta Phase II study,** which aimed to assess the safety and efficacy of estetrol (E4) for the treatment of Covid-19 hospitalized patients. E4 did not differ from placebo on the primary study endpoint, however the results further support the unique safety profile of estetrol.
- **E4 Intellectual Property:**
    - In 2021, a Supplementary patent certificate of the patent on the use of Estetrol in a combined contraceptive (EP1390042) was registered in Belgium, Finland, Italy, Luxemburg and The Netherlands. This SPC will cover the period between May 2022 and May 2027.
    - In August, **Health Canada delivered a 2-year Certificate of Supplementary Protection** for the patent on the use of Estetrol in a combined contraceptive, extending the patent end date up to May 2024. In September, the **Belgian patent office** allowed the

Supplementary patent certificate of the Belgian counterpart of the EP1390042. This SPC will cover the period between May 2022 and May 2027.

- **Obtention of an additional key patent for the product Estelle® and product candidate Donesta®** in Europe and Eurasia covering various pharmaceutical compositions, as well as their manufacturing process. This patent with an expected end date in 2036 is now granted in Japan as well and is still under prosecution in more than 50 other territories.
- The 2021 approved product Estelle® is covered by **data and market exclusivity of 8 years, 5 years and 10 years** in Canada, Europe and the United States respectively.
- The two patent applications filed following the **positive results of the Donesta® Phase II study** for the effective treatment of vasomotor symptoms are in the national phases. Once granted, these patents will consolidate and extend the protection around Donesta®.

Complex therapeutics

- **Acquisition of full licensing and distribution rights** for the Zoreline® implant indicated for the treatment of breast, prostate cancer and certain gynaecological disorders, allowing Mithra to significantly increase its margin in some of the most attractive geographies (China, Canada and Australia) outside of Mithra's former territorial scope.
- Strengthening of Mithra's business development strategy with the **complete buyout** of all remaining contingent payments obligation (earnouts) linked to Myring® and Zoreline®
- Launch of an animal **PK/PD comparative study for Zoreline®** to select final formulation for 1 month and 3 months implant. Mithra expect to launch the clinical studies end 2022/begin 2023, with a potential commercial launch in 2025.
- **Commercial launch of Myring®** in Italy (Farmitalia), Switzerland (Labatec), Poland and France (Zentiva), Chile (Pasteur) and Canada (Searchlight Pharma).
- **Commercialization agreement for Tibelia®** signed with Dampe for Venezuela and with Eurodrug in Malaysia; additional commercial launches in Chile, Switzerland, Netherlands, UAE and KSA.

Tyrosine kinases inhibitors

- **Diversification of the R&D pipeline** through rights' acquisition option relating to a development programs led by the Belgian company BCI Pharma on innovative kinase inhibitors notably indicated for the treatment of female cancers and endometriosis. Currently in the preclinical stage, BCI Pharma should initiate clinical development in 2023, with marketing authorizations expected for 2031.

Mithra CDMO

- **New manufacturing facility** fully dedicated to fill & finish production of complex liquid injectables and biologicals in vials, pre-filled syringes or cartridges.
- **Agreement with ExeVir for the manufacturing** of a novel llama-derived antibody therapies for potential treatment and prevention of Covid-19.

Corporate Governance

- **Renewal of the Board of Directors** for a two-year mandate achieving a perfect parity: 5 women directors/5 men directors, as well as 5 independent/5 non-independent directors. Mr. Ajit Shetty succeeds Ms. Patricia van Dijck as Chairman of the Board.
- **Appointment of Leon Van Rompay** as Chief Executive Officer.

Geopolitical situation in Eastern Europe

- **Monitoring of the geopolitical situation in Eastern Europe and risk assessment on Mithra's and partners activities**, in particular Estelle® launch in Russia foreseen in H2 2022. On the R&D side, we are currently analyzing the situation regarding the potential impact on the recruitment for the additional European Donesta® study (C301) that should be completed by the end of H1 2022. If needed, we will active a mitigation plan in order to switch the planned Russian recruitment sites with other sites.

Expected milestones for 2022

- **Estelle® launches** expected in additional countries, namely in Europe and Australia. New marketing authorizations are anticipated in 2022, as well as additional regulatory submissions in Latin America.
- **Donesta® primary safety results** anticipated for end 2022 in the United States/Canada and for end H1 2023 in Europe. Depending on the evolution of the Covid-19 situation, the potential impact of the geopolitical situation in Eastern Europe on recruitment, the study results and regulatory authorizations, Mithra believes it could achieve marketing authorization for Donesta® in H1 2024 for the United States and in H2 2024 for Europe.
- **Launch of 3 additional studies in Donesta® Clinical Program** (vulvovaginal atrophy, skin and hair quality) in 2022, depending on regulatory agency feedback.
- **License and supply agreement for Donesta®** for global commercial launch anticipated in 2024.
- **Launch of the clinical program on Neonatal Hypoxic-Ischemic Encephalopathy** (NHIE), a life-threatening form of neonatal asphyxia. The Phase 1 study aims to collect safety, tolerability and pharmacokinetic data with Mithra's E4-based formulation on adults. The study is expected to be initiated in H1 2022, with results anticipated in H2 2022.
- Publication of top-line results of an **ecotoxicity study** conducted at the Belgian University of Namur on the environmentally profile of contraceptive pill Estelle®.
- **Additional commercial launches for vaginal contraceptive ring Myring®** planned during the second half of the year. FDA approval for commercialization in the U.S., the largest market worldwide, by Mayne Pharma, expected in H2 2022.

FINANCIAL RESULTS

1. Consolidated statement of profit or loss

	Year ended 31 December	
Thousands of Euro (€)	*2021*	*2020*
Revenue	22,668	9,030
Cost of sales	(15,724)	(3,457)
Gross profit	**6,945**	**5,573**
Research and development expenses	(85,243)	(78,458)
General and administrative expenses	(12,515)	(15,933)
Selling expenses	(1,871)	(1,434)
Other operating income	4,809	6,574
Loss from operations	**(87,875)**	**(83,678)**
Change in fair value of contingent consideration payable	(19,265)	(18,114)
Net fair value gains/(losses) on financial assets at fair value through profit or loss	(6,351)	(4,925)
Financial income	2,838	1,782
Financial expenses	(13,116)	(5,987)
Loss before taxes	**(123,769)**	**(110,922)**
Income taxes	6,895	18,835
NET LOSS FOR THE PERIOD	**(116,875)**	**(92,086)**

2. Consolidated statement of financial position

	As at 31 December	
Thousands of Euro (€)	*2021*	*2020*
ASSETS		
Property, plant and equipment	38,354	29,921
Right-of-use assets	69,322	69,572
Goodwill	5,233	5,233
Other intangible assets	104,954	89,005
Deferred tax assets	63,456	50,905
Contract assets	49	200
Derivatives financial assets	-	6,184
Investment in equity securities	31,898	18,088
Other non-current assets	9,263	14,401
Non-current assets	**322,528**	**283,509**
Inventories	43,852	35,382
Contract assets	12,522	51,472
Derivatives financial assets	100	2,881
Trade and other receivables	10,044	10,052
Other short-term deposits	-	14
Cash and cash equivalents	32,872	138,675
Current assets	**99,389**	**238,475**
TOTAL ASSETS	**421,918**	**521,985**

	As at 31 December	
Thousands of Euro (€)	*2021*	*2020*
EQUITY AND LIABILITIES		
Share capital	32,250	31,271
Additional paid-in-capital	340,769	332,535
Other reserves	(2,545)	13,690
Accumulated deficit	(336,633)	(219,759)
Equity attributable to equity holders	**33,840**	**157,737**
Subordinated loans	11,629	12,610
Other loans	113,608	111,898
Lease liabilities	42,353	44,282
Refundable government advances	12,769	15,195
Other financial liabilities	102,675	101,180
Derivatives financial liabilities	2,897	-
Contract liabilities	-	3,706
Provisions	266	266
Deferred tax liabilities	6,089	4,363
Non-current liabilities	**292,285**	**293,500**
Current portion of subordinated loans	1,314	1,002
Current portion of other loans	45,253	10,475
Current portion of lease liabilities	6,561	7,315
Current portion of refundable government advances	1,617	1,259
Current portion of other financial liabilities	15,829	23,424
Derivatives financial liabilities	1,886	-
Trade and other payables	23,331	27,272
Current liabilities	**95,793**	**70,747**
TOTAL EQUITY AND LIABILITIES	**421,918**	**521,985**

3. Consolidated statement of cash flows

	As at 31 December	
Thousands of Euro (€)	*2021*	*2020*
Cash and cash equivalents at beginning of year	**138,675**	**49,720**
Net cash (used in)/ provided by operating activities	(74,387)	(80,025)
Net cash (used in)/ provided by investing activities	(54,682)	(16,207)
Net cash (used in)/provided by financing activities	23,245	185,187
Net increase/(decrease) in cash and cash equivalents	**(105,824)**	**88,954**
Effects of exchange rate changes on cash and cash equivalents	21	-
Cash and cash equivalents at end of period	**32,872**	**138,675**

Profit and Loss

The Group reported a net loss of EUR 116.9 million in 2021, compared to a net loss of EUR 92.1 million in 2020.

Product sales were largely driven by our first deliveries of Estelle® (EUR 13.4 million) to our European, US and Canadian partners. Sales from generic products in our portfolio, at EUR 3.8 million, remained steady compared to last year.

Out-licensing revenue, at EUR 4.6 million, are essentially Zoreline® milestones (EUR 3.7 million), previously invoiced and paid, that could be recognized in line with the agreement signed with SVR Invest BV for the full global licensing and distribution rights for the Zoreline® implant. EUR 0.5 million relates to performance obligation achieved in the framework of Mayne Pharma agreement for Estelle® Australia. Otherwise, no new significant partnership was signed during 2021 and no other triggering event on our portfolio of signed contracts, implying that no additional performance obligations (and related revenues) could be recognized in our accounts.

As anticipated, R&D expenses increased by 9% compared to last year due to Donesta® Phase III clinical studies.

G&A and sales expenses decreased by 17%, essentially due to a much lower impact of share-based payments accounting entries (charge of EUR 1.1 million compared to EUR 7.3 million in 2020).

Estelle® approval and positive top-line results from Donesta® phase 3 studies led to a review of the different scenarios and probabilities related to the financial liability against former owners of Uteron Pharma, hence the EUR 19.3 million change in fair value charge recorded in 2021 accounts.

Fair value loss on financial assets is mainly made of the charge of EUR 8.0 million related to contingent receivable with CERES, partially compensated by a fair value gain on contract assets (reevaluation of Mayne's shares up to their issuance in May 2021) for EUR 1.6 million.

Increase of net financial expenses is mostly driven by the interest charges of the EUR 125 million convertible bond negotiated in December 2020.

The group recorded a tax income of EUR 6.9 million that mainly results from the recognition of tax losses of the period in several entities as deferred tax assets, which are to be offset against future taxable income.

Alternative performance measure

Mithra decided to use some alternative performance measures (APMs) that are not defined in IFRS but that provide helpful additional information to better assess how the business has performed over the period. Mithra decided to use REBITDA[2] and EBITDA in order to provide information on recurring items, but those measures should not be viewed in isolation or as an alternative to the measures presented in accordance with IFRS.

REBITDA is an alternative performance measure calculated by excluding the non-recurring items and the depreciation & amortization from EBIT (loss from operations) from the consolidated statement of profit or loss prepared in accordance with IFRS. The Group considers share-based payments as non-recurring item above EBITDA and one-off item, impairment charges on Other intangible assets in 2020, as non-recurring item below EBITDA.

EBITDA is an alternative performance measure calculated by excluding the depreciation and amortization from EBIT (loss from operations) from the consolidated statement of profit or loss prepared in accordance with IFRS.

Financial Highlights (management figures), as referred to in previous section, can be presented as follows :

	Year ended 31 December	
Thousands of Euro (€)	*2021*	*2020*
Revenue	22,668	9,030
Cost of sales	(15,724)	(3,457)
Gross profit	**6,945**	**5,573**
Research and development expenses	(76,577)	(69,310)
General and administrative expenses	(10,021)	(8,126)
Selling expenses	(1,541)	(1,251)
Other operating income	4,809	6,574
REBITDA	**(76,385)**	**(66,540)**
Share-based payments expenses	(1,065)	(7,267)
EBITDA	**(77,450)**	**(73,807)**
Depreciation	(10,426)	(6,136)
Non-recurring items	-	(3,734)
Loss from operations	**(87,875)**	**(83,678)**
Change in the fair value of contingent consideration payable	(19,265)	(18,114)
Net fair value gains/(losses) on financial assets at fair value through profit or loss	(6,351)	(4,925)
Financial income	2,838	1,782
Financial expenses	(13,116)	(5,987)
Loss before taxes	**(123,769)**	**(110,922)**
Income taxes	6,895	18,835
NET LOSS FOR THE PERIOD	(116,875)	(92,086)

[2] Recurring earnings before interest, taxes, depreciation and amortization

Please refer to the table below for the reconciliation to loss from operations as presented within consolidated statement of profit or loss :

	Year ended 31 December	
Thousands of Euro (€)	*2021*	*2020*
Loss from operations	**(87,875)**	**(83,678)**
Depreciation	10,426	6,136
Non-recurring items – impairment charges on Other intangible assets	-	3,734
Share-based payments	1,065	7,267
REBITDA	**(76,385)**	**(66,540)**
Share-based payments	(1,065)	(7,267)
EBITDA	**(77,450)**	**(73,807)**

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Annual report 2021

The Annual Report for the year ended 31 December 2021 will be published on 15 April 2022, on the website of the Company. The auditor, BDO Réviseurs d'Entreprises SCRL, has confirmed that the audit procedure, which is substantially complete, has not revealed any material corrections required to be made to the financial information included in this press release.

Webcast

Mithra will host a conference call and live webcast today (March 8, 2022) at 09.00 CET. The live webcast can be accessed on the Mithra website or by clicking here. A replay of the webcast will be available on the Mithra investor's website shortly after the close of the call.

Financial Calendar

- 15 April 2022 : 2021 Annual Report
- 19 May 2022 : Annual General Shareholders Meeting
- 23 September 2022 : Half Year Report 2022

About Mithra

Mithra (Euronext: MITRA) is a Belgian biotech company dedicated to transforming Women's Health by offering new choices through innovation, with a particular focus on contraception and menopause. Mithra's goal is to develop products offering better efficacy, safety and convenience, meeting women's needs throughout their life span. Mithra explores the potential of the unique native estrogen estetrol in a wide range of applications in women health and beyond. After having successfully launched the first estetrol-based product in 2021, the contraceptive pill Estelle®, Mithra is now focusing on its second product Donesta®, the next-generation hormone therapy. Mithra also develops and manufactures complex therapeutics in the areas of contraception, menopause and hormone-dependent cancers. It offers partners a complete spectrum of research, development and specialist manufacturing at its technological platform Mithra CDMO. Active in more than 100 countries around the world, Mithra has an approximate headcount of 300 staff members and is headquartered in Liège, Belgium. www.mithra.com

Important information

The contents of this announcement include statements that are, or may be deemed to be, "forward-looking statements". These forward-looking statements can be identified by the use of forward-looking terminology, including the words "believes", "estimates," "anticipates", "expects", "intends", "may", "will", "plans", "continue", "ongoing", "potential", "predict", "project", "target", "seek" or "should", and include statements the Company makes concerning the intended results of its strategy. By their nature, forward-looking statements involve risks and uncertainties and readers are cautioned that any such forward-looking statements are not guarantees of future performance. The Company's actual results may differ materially from those predicted by the forward-looking statements. The Company undertakes no obligation to publicly update or revise forward-looking statements, except as may be required by law.