Document produced on
30 June 2022 at 12:27pm CET
Document published on
1 July 2022 at 8:08am CET

EQUITY RESEARCH

ABIONYX PHARMA

RESEARCH STUDY

BUY, TP of 8.1€
Up/Downside: +441%

Scaling Up

The repositioning carried out from 2019 onwards is beginning to bear fruit with promising initial study results and a growing portfolio of projects for the CER-001 molecule applied to septic shock, LCAT deficiency, ophthalmic diseases and more recently, Covid-19. The newsflow should continue to support the stock, thus reinforcing our Buy rating. Our TP of €8.1 offers an upside of over 400%.

The company was listed in 2015 under the name Cerenis Therapeutics, followed by a reorganisation phase initiated in 2019 with the entry of new shareholders in the capital. This led to the management team's evolution (Emmanuel Huynh appointed as Chairman and Cyrille Tupin as Chief Executive Officer), but above all, to reorienting and restarting research programmes focused on new indicators: renal diseases, septic shock, the ophthalmic field, etc. Subsequently, the company's corporate name was changed to Abionyx Pharma.

Since 2019, research has targeted areas with currently few or no therapeutic solutions based on the new protocols, including molecule frequency and much higher doses than in previous studies. Initial promising results have already been reported for renal diseases (LCAT orphan drug status), ophthalmic diseases, septic shock (phase IIa study in Italy financed by a consortium), and for the field of Covid-19.

In December 2021, the company announced a merger with Iris Pharma, a recognised CRO in ophthalmology (2020 revenue of €8m), bringing more than 30 years of expertise in the development of drugs and medical devices; this merger should accelerate Abionyx's development while validating the efficacy of the CER-001 molecule by a recognised professional in Ophthalmology. The merger could also lead to significant revenue in this field (horizon 2025-2026, according to us). To finance the acceleration of the research, a private placement of €4.2m was carried out last December, resulting in a cash position of €7.9m on 31 December 2021 and €5.9m on 31 March 2022.

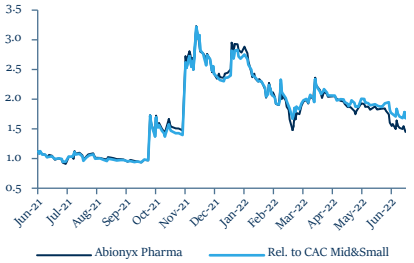
Ownership and management changes, the repositioning of research programmes, the first published results, and the merger with Iris Pharma (paid for in shares based on a value of €3.6/share in Dec. 2021) have supported the stock price's rise in recent years: x2.9 in 2019, x2.5 in 2020 and x2.5 in 2021. Since beginning-2022, the stock has fell by more than -35%, which we believe offers a strong entry point and confirms our Buy rating. Our TP stands at €8.1, representing a potential upside of over 400%.

Key data	
Price (€)	1.5
Industry	Heathcare
Ticker	ABNX-FR
Shares Out (m)	31.257
Market Cap (m €)	46.8
Next event	RN 2021 : 28/04/2022

Ownership (%)	
Domundi (E. Huynh)	11.8
Cyrille Tupin	3.3
Luc Demarre	4.5
Sadok Belmokhtar	6.8
Free float	63.2

EPS (€)	12/22e	12/23e	12/24e
Estimates	-0.26	-0.37	-0.32
Change vs previous estimates (%)	na	na	na

Performance (%)	1D	1M	YTD
Price Perf	-5.4	-20.0	-38.8
Rel CAC Mid&Small	-5.4	-12.1	-27.8



TP ICAP Midcap Estimates	12/21	12/22e	12/23e	12/24e
Sales (m €)	0.7	6.7	7.8	11.3
Current Op Inc (m €)	na	na	na	na
Current op. Margin (%)	-881.8	-117.2	-160.5	-106.5
EPS (€)	-0.21	-0.26	-0.37	-0.32
DPS (€)	0.00	0.00	0.00	0.00
Yield (%)	0.0	0.0	0.0	0.0
FCF (m €)	-6.9	-8.9	-12.9	-12.2

Valuation Ratio	12/22e	12/23e	12/24e
EV/Sales	7.1	6.2	4.3

Consensus FactSet - Analysts:1	12/22e	12/23e	12/24e
Sales	8.2	9.4	na
EBIT	-4.4	-6.8	na
Net income	-4.7	-7.2	na

Analyst
Claire Deray - Sponsor Finance for TPICAP Midcap

Description

Using active ingredients developed by Cerenis Therapeutics, notably a recombinant HDL molecule (high-density lipoprotein, often referred to as the good cholesterol), Abionyx Pharma has redirected the research programmes towards new indications such as kidney diseases, certain metabolic disorders, and opthalmic disease (acquisition of Iris Pharma at the end of 2021).

SWOT Analysis

Strengths

- Portfolio of patents
- CER-001, one of the most advanced bioproducts (HDL mimetic)
- Mastery of the production phases
- Healthy financial situation

Weaknesses

- A troubled operational and stock market track record
- A team that remains small
- A refocusing on new indications that remains embryonic (launch of Phase IIa trial for the most advanced project)

Opportunities

- New indications for CER-001
- HDL platform as a vector for administering other molecules or treatments
- Partnership in PPAR

Threats

- New failure in R&D efforts
- Inability to conclude new partnerships (research, product development, marketing, etc)
- Need to secure financing to accelerate research programmes

Overview: A Successful Repositioning

Founded in 2005, and listed on the stock exchange in 2015, Cerenis Therapeutics became Abionyx Pharma in June 2019. Thanks to fundraising of more than €170m from institutional investors: mainly Sofinnova, HealthCap, Alta Partners, BPI France, TVM Life Science, Wyss, the public offering (€53.4m raised at the time of the IPO of €12.7/share), Cerenis Therapeutics was able to carry out research programs enabling:

- The identification and metabolise of a compound comprised of a natural HDL protein, apolipoprotein A-I (apoA-I) and phospholipids (one of which is negatively charged): molecule CER-001, which has promising properties.
- The execution of the necessary tests for this molecule's production (cell culture in a bioreactor, outsourced production).
- Proof of the molecule's safety via advanced studies until the end of phase III showing no (or few known) side effects.
- Filing for several patents and patent families to protect the company's intellectual property.
- The discovery other molecules such as a specific agonist of the peroxisome proliferator-activated receptor delta (PPAR), the molecule CER-002; a P2Y13 receptor agonist, the molecule CER-209 (Nash's disease), or an HDL mimetic based on an apoA-I analogue peptide, the molecule CER-522 (aortic valve stenosis).

Despite efforts of teams in France and the United States, as well as the products' promising properties, the clinical studies initiated for several disease indicators, such as post-acute coronary syndrome (Carat study), oesophageal cancer (Target study), or patients suffering from Primary Hypercholesterolemia (an orphan disease, TANGO study), did not demonstrate the efficacy of certain molecules.

At the beginning of 2017, following the first unfavourable results from clinical studies (phase II of the Carat study), the founding directors decided to significantly reduce investments and redirect them towards new indicators (NAFLD and NASH). At the same time, they adapted the group's structure by closing the US subsidiary, changing the head office, and halving the number of employees to seven.

After some setbacks concerning the research for new targeted indicators (imaging studies), and the failure of the merger with H4 Orphan Pharma (a biotech focused on the development of therapies for lung diseases), a new phase of reorganisation was initiated in 2019. This included the arrival of new shareholders, a management shake-up, and in particular, a repositioning and relaunching of new research programmes.

Repositioning initiated in 2019

New shareholders, management changes and new developments

In order to finance its repositioning, the group has raised several funds (€1.0m in 2019 at €0.32/share and €1.9m in 2020 at €0.69/share) leading to the entry of new shareholders, management changes (Emmanuel Hyunh appointed as Chairman and Cyrille Tupin as CEO), research programme launches on new indicators, and ultimately, a new corporate name, Abionyx Pharma.

The new management team conducted a review of Cerenis Therapeutics' legacy product and patent portfolio. As a result, they decided to focus their research on the molecule CER-001 (HDL mimetic) and its promising properties, and on the molecule CER-002 via partnerships.

Among the possible fields of application for HDL molecules, management has targeted specific areas of new research, fields for which there are few or no therapeutic solutions at present. These programmes are based on new protocols, including higher molecule frequency and doses compared to previous studies. Research has shown that HDL plays a major anti-inflammatory role and impacts kidney functionality. Significant effects were observed in an animal model of genetic kidney failure. Several other models have shown that HDL stimulates renal remodelling, a critical factor contributing to the progression of pathologies. Based on this evidence, management decided to target severe indicators concerning liver disease.

In order to provide the necessary doses for future research programmes, CER-001 molecule production was relaunched in 2020. To ensure product availability and CER-001 molecule supply, at end-2020, the decision was made to relocate sourcing to France. In March 2021, Abionyx announced a partnership agreement with Fareva / GTP Biologics, based in Saint-Julien-en-Genevois, and V-Nano, based in Toulouse, both specialists in biomanufacturing in France.

By 2020, initial promising results were reported for kidney disease, followed by success regarding ophthalmologic disease in March 2021.

CER-001 for a very rare kidney conditions: LCAT deficiency

In a preclinical study, Professor Laura Calabresi, a world expert in the field of HDL and professor at the University of Milan, provided proof of CER-001's efficacy regarding a rare kidney disease: LCAT deficiency (2018-2019, publication end-2020). Following these initial results, the company continued its kidney disease work, obtaining a Temporary Authorisation for Use (TAU) for CER-001

applied to rare kidney disease with no existing treatment, delivered in January 2020 in France (Professor Stanislas Faguer, nephrologist at the Toulouse-Rangueil University Hospital and member of the Reference Centre for Rare Kidney Diseases) and in February 2020 in Italy.

As early as November 2020 (preclinical results published in the journal Metabolism on 15 December 2020), the company published the first test results conducted for this molecule. Given the disease's severity, the patients included in the study (in France and Italy) were on the verge of receiving dialysis (medical technique for purifying blood when the kidneys no longer perform this function), which was halted during their CER-001 treatment. Additionally, a French patient also developed corneal lipid deposits. Following the treatment, the visual blur caused by the corneal deposits disappeared.

These results were confirmed for the French ATU patient in the Annals of Internal Medicine in March 2021 and for the Italian ATU patient in the Journal of Internal Medicine in November 2021.

The CER-001 test results confirmed:

- excellent patient tolerance to the drug (despite more frequent, higher doses than in previous clinical trials)
- a potentially modifying effect on the progression of severe renal disease, which could offer a therapeutic option to patients for whom there is no treatment
- the molecule's systemic action, with a probable effect on ophthalmic lipid deposits

Based on the strength of the initial results, management's strategic decisions were confirmed: focus on CER-001 for certain renal and ophthalmic diseases, for which an initial phase IIa study for renal diseases was launched at end-2020 in Italy.

CER-001 for septic patients: Racers randomised Phase IIa study

The first indicator targeted in by the company's research concerns patients suffering from kidney damage leading to Acute Kidney Injury (AKI) following septic shock. Septic shock is an acute circulatory failure manifested by a sudden drop in blood pressure, commonly caused by a bacterial infection (though sometimes viral or fungal (yeast)). During septic shock, organs will be unevenly supplied with blood, which may result in their dysfunction, particularly the kidneys, which are very much in demand to eliminate bacteria or other causes of septic shock. Following a septic episode, some patients have serious complications, including acute renal failure, as the kidneys are no longer able to eliminate metabolic waste, which can lead to patient death.

Based on the initial results of the UTAs, the group obtained authorisation from the Italian regulatory authorities at end-2020 to launch a clinical study in partnership with the University of Bari, and the support of two KOLs (Key Opinion Leaders): Professor Loreto Gesualdo (Head of Nephrology, Dialysis and Transplantation Unit) and Professor Salvatore Grosso (Head of Anaesthesia and Intensive Care Unit).

The phase IIa RACERS study (Randomised - CER-001 - Septic patients) has thus been launched, targeting patients with sepsis at high risk of developing acute kidney injury. The study will involve a cohort of 20 patients with trial doses designed to optimise the compound's effects. Patients will receive 8 doses over 6 days, with three ascending series (low, moderate and high), or a placebo. The study's objective is to verify the compound's safety and tolerability at the targeted doses, and to determine the optimal dose of CER-001 to be administered for the next stage of the clinical trial (Phase IIb). The first patient was enrolled in June 2021 at a specialised centre in Italy.

This study is fully funded by the CBVF consortium (estimated cost €5-10m). The CBVF (Consorzio per Valutazioni Biologiche e Farmacologiche, or the Italian Consortium for Biological and Pharmacological Evaluation) provides scientific, methodological and regulatory support to European entities and companies wishing to innovate in the pharmaceutical and biotechnological fields. Abionyx retains full intellectual property rights on the research. Within the framework of this partnership, CER-001 doses will be made available free of charge to the physicians participating in this study.

CER-001 for ophthalmic disease

In the context of research conducted on patients with a mutation of the LCAT gene, as early as end-2020, the group had obtained promising initial results for ophthalmology for a French patient, who experienced improvement in visual blur after a few weeks of treatment. The results suggested the anti-inflammatory and/or reverse cholesterol transport-enhancing properties of CER-001 may improve vision in patients with LCAT activitý deficiency, commonly referred to as 'fish eye'.

This discovery, and previous data showing the role of apoA-I in the development of corneal opacification and corneal lipid deposits, paved the way for pre-clinical studies testing CER-001 for ophthalmic diseases.

2021: Everything accelerates...

Orphan drug status granted for LCAT deficiency

- *Results of the French study published in March 2021*

The French study, which began in January 2020 by Professor Stanislas Faguer at the Toulouse University Hospital, involved a patient with low circulating levels of HDL and apoA-I, with rapidly progressive kidney disease. The patient received an intravenous dose of 10mg/kg 3 times a week for 3 weeks, then twice a week for 3 weeks and once a week for 3 weeks. Subsequently, the dose was increased to 20mg/kg/week for 6 weeks to reach the dose that stabilised the kidney's estimated Glomerular Filtration Rate (eGFR). GFR is a parameter used to study the kidney's state of functionality: a GFR between 90 and 60 ml/min/1.73 m2 expresses the existence of early renal insufficiency; a GFR between 60 and 30 ml/min/1.73 m2 moderate renal insufficiency; a GFR lower than 30 ml/min/1.73 m2 connotes severe or very severe renal insufficiency.

In the 9 months prior to the study, the patient's eGFR had rapidly decreased from 41 to 19 ml/min/1.73m2. In the 11 months following the introduction of CER-001 treatment, eGFR only decreased from 19 to 17 ml/min/1.73m2.

During the treatment period (5.5 months), proceeded by a one-year follow-up, the patient's renal functionality stabilised, thus avoiding dialysis.

The French patient had also developed corneal lipid deposits. Following the CER-001 treatment, the visual blur caused by the corneal deposits disappeared. This improvement in visual function was still observed after one-year follow-up.

As the patient had not received any other treatment during this period, the arrest of the renal decline and improvement in visual functionality can most likely be attributed to the administration of CER-001.

- *Orphan drug designation in September 2021*

Following these very promising results, management decided to carry out further development regarding this disease; it obtained orphan drug status for the CER-001 molecule for the LCAT indicator (ultra-rare disease), for both renal and ophthalmic diseases.

The project received a positive review from the Committee for Orphan Medicinal Products (COMP) of the European Medicines Agency (EMA) in July 2021; the orphan drug designation was obtained in September 2021, only a few months after the first results of patients treated under ATU. Management has obtained orphan drug designation for CER-001 in the two targeted areas, namely for the renal and ophthalmic indicators.

At the European level, orphan drug status leads to access to an accelerated marketing process (centralised procedure), technical support, reduced regulatory costs and 10 years of protection in Europe once marketing authorisation is obtained.

- *Results of the Italian study published in November 2021 in the Journal of Internal medicine*

In February 2020, Dr Laura Calabresi obtained a UTA for a 49-year-old patient with an LCAT gene mutation who had developed aggressive glomerulus -therapy that had required three separate kidney transplants over 20 years.

At the time of the study's initiation, the patient had very low HDL cholesterol and abnormally high lipoprotein complexes, called LpX, which are known to be toxic to the kidney. With 12 weeks of treatment (infusions of CER-001), the lipoprotein profile was normalised, with a decrease in abnormal LpXs in favour of normal-sized lipoproteins. Lipid deposits were reduced in the kidney and the disease's progression was halted.

The evidence gathered demonstrates the molecule's potential, and its application to other kidney diseases, thus constituting new therapeutic fields.

<u>New ophthalmological indicators and the Iris Pharma merger</u>

- *October 2021: Publication of pre-clinical results for uveitis*

In the framework of the French ATU in LCAT, the intravenously administered CER-001 made it possible to avoid putting the test patients on dialysis, as well as the elimination of visual blur. The improvement in visual functionality was still observed after the one year follow-up.

Aware of the role of lipids in ocular pathologies, management then decided to launch a preclinical study for the ophthalmic model. The molecule proved to be safe and well tolerated for ocular surface administration (as drops), inside the eye (injection into the vitreous), or via intravenous injection.

The molecule has also been shown to be effective in uveitis (eye inflammation) caused by injection of lipopolysaccharide into the vitreous (measurements of protein concentration and cellular infiltration in the aqueous humour). Based on the preliminary results, and with the support of prominent practitioners (Professor Catherine Creuzot-Garcher, Professor of Ophthalmology in Dijon, Head of the Ophthalmology Department at the University Hospital of Dijon, University Professor, co-leader of the Eye, Nutrition and Cellular Signalling team at the Centre des Sciences du Goût et de l'Alimentation in Dijon, and Dr. Niyazi Acar, head of the Eye, Nutrition and Cell Signalling team at the Dijon Taste and Food Science Centre, management announced its intention to launch research programmes for the development of a new class of drugs (HDL mimetics) for ophthalmology pathologies that create lipidic corneal deposits, and a

project partnership with a company specialised in this sector, Iris Pharma, the company that conducted the preclinical studies for uveitis.

- *December 2021: Cooperation with a CRO and Ophthalmology specialist*

Last December, the group acquired 100% of Iris Pharma's capital. In view of the results obtained with the CER-001 molecule, management and shareholders of Iris Pharma decided to join Abionyx's project by selling their company in exchange for shares (3.4% of the capital) and a premium for 2024 objectives based on clinical study results).

Iris Pharma is a French CRO (Contract Research Organisation) based in Nice and specialised in pre-clinical and clinical studies in the field of ophthalmology. During its 32-year history, the company has participated in numerous studies that have allowed it to test more than 5,000 molecules, leading to the market launch of approximately 70 treatments and products.

Iris Pharma offers in vivo efficacy and bio-analysis services, applies GLP (Good Laboratory Practice) principles for pre-clinical studies, conducts clients' clinical studies (phase I to IV, in Europe, North America and Asia), carries out marketing studies and offers consulting services (support in determining the best molecule indicator or product).

Iris Pharma's management has remained in the hands of Yann Quentric, who will continue the company's historical CRO activity; its founder, Dr. Pierre-Paul Elena, will join the Abionyx teams to lead the targeted development projects as CSO (Clinical Studies Officer). Cyril Tupin will remain as CEO of the new entity, which has subsequently changed scale.

... and is confirmed by the newsflow at the beginning of 2022

January & March: testing of the CER-001 molecule in the fight against Covid-19

Observed in COVID-19 patients with acute lung injury that can progress to acute respiratory distress, was a decrease in cholesterol, LDL (Low Density Lipoproteins) and HDL (High Density Lipoproteins) levels. Patients with low HDL levels at hospital admission had an increased risk of developing severe disease compared to patients with high HDL levels. Recovery from COVID-19 infections, serum lipid levels return to pre-infection levels.

Boosting HDL levels by injecting CER-001 could be one way to accelerate patient recovery from Covid-19, a condition for which there is currently no suitable treatment. The company has obtained an Authorisation for Compassionate Access (equivalent to ATUn, Autorisation Temporaire d'Utilisation nominative) from the French National Agency for Medicines to use the HDL CER-001 bio-molecule in the treatment of hospitalised Covid-19 patients (company press release from January).

In an article in the journal biomedecines published on the MDPI website in March, professionals from Hospital Bichat reported on the initial conclusions of the use of Abionyx's HDL biomolecule CER-001 for the treatment of a severe COVID-19 (for patients in intensive care) by infusion. Assessment of inflammatory markers and cytokines showed mostly a significant decrease upon infusion of recombinant HDL, suggesting that its use is feasible, and is a potential therapeutic strategy to be explored for COVID-19 patients.

March: FDA orphan drug designation for the LCAT

Following the green light from the European authorities obtained in September 2021, last March, executives announced that they obtained orphan drug designation for CER-001 for the indication of LCAT deficiency (an ultra-rare disease that can involve severe kidney and eye conditions) from the FDA (US regulatory authority) for an ophthalmic indicator (fish eye, lipid deposit in the eye that opacifies the cornea and eventually requires a transplant) and a renal indicator (renal failure leading to dialysis or even a renal transplant.

In the US, the designation also provides access to tax credits for clinical trials, a user fee waiver and 7 years of market exclusivity after approval.

April: First results from the RACERS study

Finally, in April, the group published the first results of the Phase IIa clinical trial, the RACERS study conducted in Italy, for patients with sepsis and a high risk of developing acute kidney injury. In the study's first ten patients, the following effects were demonstrated:

i) the rapid reversal of cytokine cascade

ii) rapid improvement in inflammation biomarkers, with

iii) no severe side effects (doses of 5, 10 and 20 mg/kg, twice daily), preventing the decline of septic patients to acute kidney injury (clinical benefit demonstrated as early as day 3)

Although this publication is only the first step in this phase IIa study, the initial results bode well for the continuation of the process: finalisation of the inclusion of patients (20 patients targeted by the study, 7 still to be included due to the Covid delay) and publication of the final results before moving on to the next phases.

These results are very promising and, if confirmed, could provide a solution for the treatment of sepsis, but also for other severe and acute inflammatory diseases.

A Company Changing Scale

A growing product development pipeline

Further studies in the renal field

- *Marketing authorisation expected within 2 years for CER-001 regarding LCAT deficiency*

The designation of orphan drug status obtained in September 2021 in Europe and in March 2022 in the United States, allows access to an accelerated marketing process (centralised procedure), technical support, reduced regulatory fees and a 10-year protection on the European territory as soon as the marketing authorisation is obtained. This classification is expected to accelerate new NDAs and market entry steps.

Management also indicated that they have received several applications for a new regulatory approval for CER-001 for the LCAT indicator (25 in Europe and the US), which, combined with the orphan drug status and the disease's very rare occurrence (probably only a few cases in the study), should lead to a rapid green light to market CER-001 for this indicator. We expect to see the first revenue for this indicator as early as 2023, with marketing authorisation expected in 2024, according to our scenario.

- *Results of the Racer study for septic shock*

Although the first patient was recruited in June 2021, the influx of Covid-19 patients disrupted the pace of patient inclusion due to overcrowded intensive care units. However, as the study's targeted treatment could be administered over only a few days with rapidly appearing effects, the first results were published in April for the first ten patients.

With a total of 20 patients in the study, its final results are expected in the autumn. In view of the results published for the first 10 patients, the group should begin phase IIb of the study before end-2022. As with Phase IIa (fully funded by an Italian consortium), we believe it is likely that the group will team up with one or more partners to continue studies in this field.

Given the duration of the clinical trials (phase IIb and phase III, 2023-2024) and regulatory stages (2025), we believe that the commercialisation of CER-001 for septic shock could come by 2026.

New intentions in Ophthalmology

The Iris Pharma acquisition brings with it a team of 60 people (vs. less than 10 people at Abionyx) with more than 30 years of know-how in the development of drugs and medical devices for ophthalmic diseases. This expertise should accelerate Abionyx's developments in the field, but above all it validates the efficacy of the CER-001 molecule for these new indicators by a recognised professional in the sector (more than 400 customers). This should very likely facilitate market penetration once the necessary authorisations are obtained.

With this transaction, management aims to develop a portfolio of first-in-class HDL bioproducts in the field of ophthalmology, targeting 3 new biopharmaceutical candidates that could enter the clinical phase, and 14 ophthalmology indicators such as uveitis, dry eye, AMD, diabetes-related ophthalmic conditions, etc., which affect many people worldwide.

In addition to the targeted indicators, work will focus on the use of injectable CER-001 (intravitreal or in the optic nerve), in drop form or in systemic form (drugs). But also as a "combo", i.e. as a vector for the administration of other active ingredients (known to be poorly soluble or lipophilic) thanks to the properties of the HDL molecule.

Although the main development areas have already been identified, Dr Pierre-Paul Elena's expertise and the support of the Iris Pharma teams will be key to selecting and arbitrating the programmes to be completed, or at least prioritised, which we believe will lead to rapid market launches.

Compared to other healthcare sectors, development times and costs in ophthalmology are reduced: toxicity, for example, is measured at 28 days vs. several months for other categories of drugs; cohorts are also smaller.

In this specific segment, given the track-record of Abionyx's CER-001 molecule combined with Iris Pharma's know-how, we believe that the group could launch its first ophthalmology product as early as late 2024 or early 2025, with subsequent products following in 2025-2026. The budget stands at around €10m per product.

The group has already announced on ongoing research in the field of uveitis (preclinical phase and phase I completed) for the CER-001 molecule, but other indicators are in the preclinical phase for corneal disorders, as well as in combination with other molecules thanks to the HDL molecule's transport properties.

Promising advances for Covid-19 patients

- *Expanded access announced in January*

In January, the company announced that it had received an Authorisation for Compassionate Use (AAC) from the French National Agency for Medicines and Health (ANHM) for the use of the HDL biomolecule CER-001 in the treatment of hospitalised Covid-19 patients.

A decrease in cholesterol, LDL (Low Density Lipoproteins) and HDL (High Density Lipoproteins) levels has been observed in patients with COVID-19 infections (acute lung injury that can progress to acute respiratory distress). Patients with low HDL levels on hospital admission had an increased risk of developing severe disease compared to patients with high HDL levels. With recovery from COVID-19 infections, serum lipid levels return to pre-infection levels.

Boosting HDL levels through CER-001 molecule injection could be one way to help patient recovery from Covid-19, a condition for which there is currently no suitable treatment.

- *First results published in March*

In the conclusion of the *Biomedecines* paper published in March 2022, it is stated that data shows for the first time that intravenous HDL supplementation is feasible in acute inflammatory conditions such as COVID-19, with a tendency to limit inflammation. This case report encourages a randomised placebo-controlled study to evaluate the contribution of bio-HDL in patients with severe COVID-19.

CAAs in Covid-19 are involved in the field of resuscitation, where the company is already conducting the RACERS study in Italy. The knowledge of the resuscitation field is clearly an asset in the conduct of these CAAs, which could lead to a larger study (which will probably be conducted in partnership). But above all, it could bring hope for this condition's treatment, one affecting the entire world. However, it is still too early to integrate these factors into our model.

Other potential indicators

- *For the molecule CER-001: use of the molecule's natural transport properties in the body and possible indicators in other kidney diseases*

As natural carriers, HDLs specifically target cellular receptors, so they can be used as vectors to increase drug efficacy and minimise side effects. Endogenous HDL has been extensively researched as a carrier for the delivery of active ingredients such as anti-cancer molecules, peptide or non-peptide antigens, nucleic acids (microRNAs, interfering RNAs, antisense oligonucleotides, etc.), markers (fluorescent or radioactive) and others (vitamins, antioxidants).

TARGET, the clinical study initiated at the end of 2017, evaluates CER-001's potential to visualise tumours in cancer patients, validating the use of HDL nanoparticles for the delivery of drugs specifically targeting tumour cells. Management is now exploring the possibility of using the CER-001 molecule as a treatment delivery vehicle. This could be applied in areas as diverse as vaccinations, infectious diseases, metabolic diseases and oncology including immuno-oncology and chemotherapy.

Given the effects obtained on the corneal lipids of the French patient, and the problems associated with the administration of certain molecules in ophthalmology, CER-001 could be used in combination with other active ingredients to participate in the development of new ophthalmology treatments in partnership with the sector's specialists.

The March 2021 publication also mentions that the effects of CER-001 on the decline of renal function should be evaluated in the more common proteinuric diseases (presence of proteins, most often albumin, in the urine), including diabetic nephropathy (kidney damage due to diabetes and high blood pressure) or extra-membranous glomerulonephritis (thickening of the glomerular basement membrane that can lead, among other things, to kidney failure), both of which are characterised by reduced local LCAT activitý, glomerular lipid deposits, and inflammatory processes, or other nephropathies (kidney diseases) associated with lipid deposits. The company is exploring other avenues of research for its CER-001 molecule within the field of renal disease.

- *For CER-002: PPARδ*

CER-002 was developed from novel chemical entities that are specific agonists of human PPARδ, a multifaceted therapeutic target. It has been selected for clinical development from a range of available small molecules under a licensing agreement with Nippon Chemiphar Co, Ltd. Abionyx acquired the rights for Europe and North America in 2005, while Nippon Chemiphar retained the rights for Asia (possible licensing for Asian rights).

The Phase I clinical study showed:

- Control of chemical synthesis and manufacturing to cGMP standards
- Pharmacological efficacy in humans as well as confirmed safety and tolerability
- Better efficacy for CER-002 compared to other previously developed PPAR delta agonists

The company is now ready to launch phase II of its research programmes based on the CER-002 molecule, directing the work towards new indicators: renal diseases (using patent applications to protect research in this field) such as dyslipidaemia (dysfunction of lipid metabolism leading to abnormally high levels of fat in the body) or renal inflammation. The work will be carried out through partnerships. Indeed, the company will not launch its PPAR development alone.

The relaunch of development and research programmes has had a slight impact on the company's results over the last two FYs, but the losses incurred and the investments made have remained under control, allowing the group to retain its strong financial health.

A healthy situation

2021's higher operational losses due to research's relaunch

Faced with the first inconclusive results of clinical studies in early 2017, R&D expenses and administrative and commercial costs were significantly reduced, enabling operating losses to be limited to -€6.6m in 2017 and -€7.2m in 2018 (including €1.4m of provisions related to restructuring), vs. -€24m in 2016 and -€15.5m in 2015 (acceleration of investments following the funds raised through the IPO).

A second wave of reorganisation led by the new management team (discontinuation of certain research, staff reductions) has enabled operating losses to be reduced again, falling to -€2.4m in 2019. In 2020, relaunching the research programmes (CER-001 molecule in particular) was accompanied by an increase in R&D costs, which was largely offset by a further reduction in administrative and commercial costs, enabling operating losses to be contained at -€3m.

In 2021, the group recorded revenue of nearly €700k thanks to the consolidation of Iris Pharma in December and to a lesser extent the first sales of the CER-001 molecule in the context of the CAA (€27k). However, due to the diversification of targeted indicators, on one hand, and the re-launch of CER-001 molecule batch production on the other, operating losses increased to -€5.8m. It should be noted that excluding the effect of bonus share plans (impact of €0.8m on the income statement), administrative and commercial expenses were virtually stable. Additionally, given the increase in R&D expenditures (€5.6m vs. €2.3m in 2020), the Group should benefit from an increase in the Research Tax Credits: €1.8m targeted for 2021, vs. €0.6m for 2020.

Income statement summary

M€	2014	2015	2016	2017	2018	2019	2020	2021
Sales	**0,0**	**0,0**	**0,0**	**0,0**	**0,2**	**0,0**	**0,0**	**0,7**
G&A expenses	-2,6	-2,8	-7,0	-1,2	-2,3	-1,8	-1,2	-2,2
R&D expenses CIR excl.	-4,3	-14,7	-20,6	-4,9	-3,7	-0,7	-1,7	-3,8
CIR	1,2	2,1	3,6	1,3	1,2	1,7	0,6	1,8
EBITDA	**-5,7**	**-15,4**	**-24,0**	**-6,1**	**-5,8**	**-2,5**	**-2,9**	**-5,8**
Depreciation and amortisation	-0,3	-0,1	0,0	-0,6	-1,4	0,0	0,0	-0,1
EBIT	**-6,1**	**-15,5**	**-24,0**	**-6,6**	**-7,2**	**-2,5**	**-3,0**	**-6,0**
Financial result	-0,5	-1,2	-0,8	1,7	0,7	4,4	1,2	0,1
NP	-6,6	-16,6	-24,9	-5,0	-6,5	1,8	-1,9	-5,8
Corrected NP*	-6,6	-16,6	-24,9	-5,0	-5,0	-3,0	-3,1	-5,8

* Adjusted for reorganisation costs in 2019 and the waiver of BPI claims in 2019 and 2020 Source: Company

Income recognised in 2019 and 2020, €4.9m and €1.1m respectively, mainly from the waiver of receivables from the BPI: a repayable advance granted in 2010 for research in the treatment of cardiovascular diseases for products recognised in 2019 (CER-001 molecules, declaration of technical failure of the project), and a repayable advance granted in 2012 for research work in the field of liver fibrosis (NAFLD and NASH, CER-209 molecule, declaration of the project's technical failure).

Restated for the exceptional items in the past, the net loss generated by the group amounted to -€5.8m in 2021, after -€3m in 2019 and -€3.1m in 2020, leading to recourse to external financing, mainly through capital increases.

Regular fundraising to maintain the group's financial health

Thanks to the strong control of operating losses, the absence of Capex (research costs fully expensed as operating expenses) and the funds raised via capital increases, the company has maintained its strong financial health.

In 2019 and 2020, the group raised several funds (€1.0m in 2019 at €0.32/share and €1.9m in 2020 at €0.69/share) leading to the entry of new shareholders (Domundi represented by Emmanuel Huynh, Luc Demarre and Christian Chavy), the reinforcement of Cyrille Tupin's shareholding, and the exit of long-standing shareholders (Sofinnova, Health Cap, Alta Partners).

In 2021, the group acquired Iris Pharma at the end of the year (included in the year-end balance sheet but not in the income statement), valued at €5m, to which must be added a debt assumption, giving an estimated enterprise value of €7m (excluding rental debt included in the IFRS accounts for nearly €2.7m). The payment was made in shares, based on a price of €3.6/Abionyx share (nearly 2.5x the last closing price before the announcement), leading to the creation of 1,388,888 Abionyx shares (vs. 24,644,664 shares before the transaction), for a little less than 6% of shares.

To support Ophthalmology projects, in early December 2021, a €4.2m private placement was carried out (partly subscribed by the historical investors), based on Iris Pharma's transaction price of €3.6/share, thus limiting the dilution for existing shareholders and creating 1,169,445 additional shares.

During the last FY, Iris Pharma's main shareholders, Pierre-Paul Elena (founder) and Yann Quentric (manager of the company), acquired 1.3% and 2.2% of Abionyx's capital respectively. Additionally, a threshold crossing was declared: Sadok Belmoktar, with 6.8% of the capital.

Over the last 3 years, almost all of the shareholders have been renewed. Only one of the founders, and former manager, Jean-Louis Dasseux, still holds a 4.7% stake (number of shares unchanged but diluted by the various fund-raising operations).

Recent shareholding changes

	31/12/18		31/12/19		31/12/20		31/12/21	
	No of shares	% capital	No of shares	% capital	No of shares	% capital	No of shares	% capital
Domundi (E. Huynh)	-	-	2 218 750	10,1%	2 986 865	12,1%	3 195 198	11,4%
Cyrille Tupin	147 806	0,8%	460 306	2,1%	837 117	3,4%	906 561	3,2%
Jean-Louis Dasseux	1 286 781	6,8%	1 286 781	5,9%	1 286 781	5,2%	1 286 781	4,6%
Sofinnova	1 535 605	8,1%	-	-	-	-	-	-
HealthCap	943 037	5,0%	943 037	4,3%	943 037	3,8%	943 037	3,4%
Alta Partners	824 701	4,4%	824 701	3,8%	824 701	3,3%	824 701	3,0%
BPI France	1 630 451	8,6%	1 630 451	7,4%	1 630 451	6,6%	1 630 451	5,8%
TVM Life Science	1 213 439	6,4%	1 213 439	5,5%	1 213 439	4,9%	1 213 439	4,3%
Luc Demarre	-	-	468 750	2,1%	896 286	3,6%	1 104 619	4,0%
Christian Chavy	-	-	-	-	173 913	0,7%	207 246	0,7%
Sadok Belmoktar	-	-	-	-	-	-	1 859 098	6,7%
Pierre-Paul Elena	-	-	-	-	-	-	347 222	1,2%
Yann Quentris	-	-	-	-	-	-	586 110	2,1%
Others	11 279 993	59,5%	12 900 801	58,8%	13 850 074	56,2%	13 809 811	49,5%
Total	**18 947 016**		**21 947 016**		**24 642 664**		**27 914 274**	

Source: Company

In 2020, the company obtained the reimbursement of the 2018 and 2019 research tax credits amounting to €1.7m, and benefited from the debt waiver (€0.9m). In 2021, fundraising only partially compensated for the cash requirements. In addition, the integration of Iris Pharma's cash led to a cash inflow of €1.5m. At the end of December 2021, free cash flow was €7.9m vs. €9.2m at the end of 2020, and net cash flow was €3m (debt from the consolidation of Iris Pharma, including €2.7m of rental debt) and €9.1m respectively.

Cashflow statement and changes in net position

M€	2014	2015	2016	2017	2018	2019	2020	2021
Cash flow	-4,9	-14,9	-18,5	-8,2	-5,7	-2,6	-2,7	-4,9
Capex	0,0	0,0	0,0	0,0	0,0	0,0	-0,1	-0,2
Change in WCR	1,6	1,2	-0,7	-0,9	-0,3	-1,3	2,1	-1,7
FCF	**-3,3**	**-13,7**	**-19,2**	**-9,1**	**-6,0**	**-4,0**	**-0,7**	**-6,9**
Disposals	0,0	0,0	0,0	0,0	0,0	0,0	0,0	0,0
Financial invesments	0,0	-0,2	0,0	-0,2	0,0	0,0	0,0	1,5
Dividends	0,0	0,0	0,0	0,0	0,0	0,0	0,0	0,0
Others	0,0	0,0	0,0	0,0	0,0	0,0	0,0	0,0
Cash excess (deficit)	**-3,3**	**-13,9**	**-19,2**	**-9,3**	**-6,0**	**-4,0**	**-0,8**	**-5,4**
Change in debt	0,0	0,0	0,0	0,8	0,0	-0,2	-0,2	0,0
Change in equity	0,0	49,0	0,9	0,2	1,2	1,0	1,8	4,0
Change in cash	-3,3	35,1	-18,3	-8,4	-4,8	-3,1	0,8	-1,4
Cash available	7,8	43,0	24,7	16,3	11,5	8,3	9,2	7,9
Net cash	**2,9**	**36,9**	**17,6**	**10,0**	**6,0**	**7,1**	**9,1**	**3,0**

Source: Company

Promising prospects

Only three years after repositioning the research programme towards two of the portfolio's molecules, the study phase pipeline has already been significantly expanded. In view of the results of the first preclinical studies, together with the potential for other indicators that have yet to be targeted, the pipeline could continue to grow, fuelling future newsflow.

Furthermore, given the strategic choices (orphan drug status, rapprochement with a CRO in the ophthalmology, etc.), the timeframe for launching the first products on the market has moved closer; subsequently, the company has changed scale.

In return, we believe that this will imply a further acceleration of R&D and product sourcing expenditures, which should initially impact the company's operational performance and require recourse to external financing.

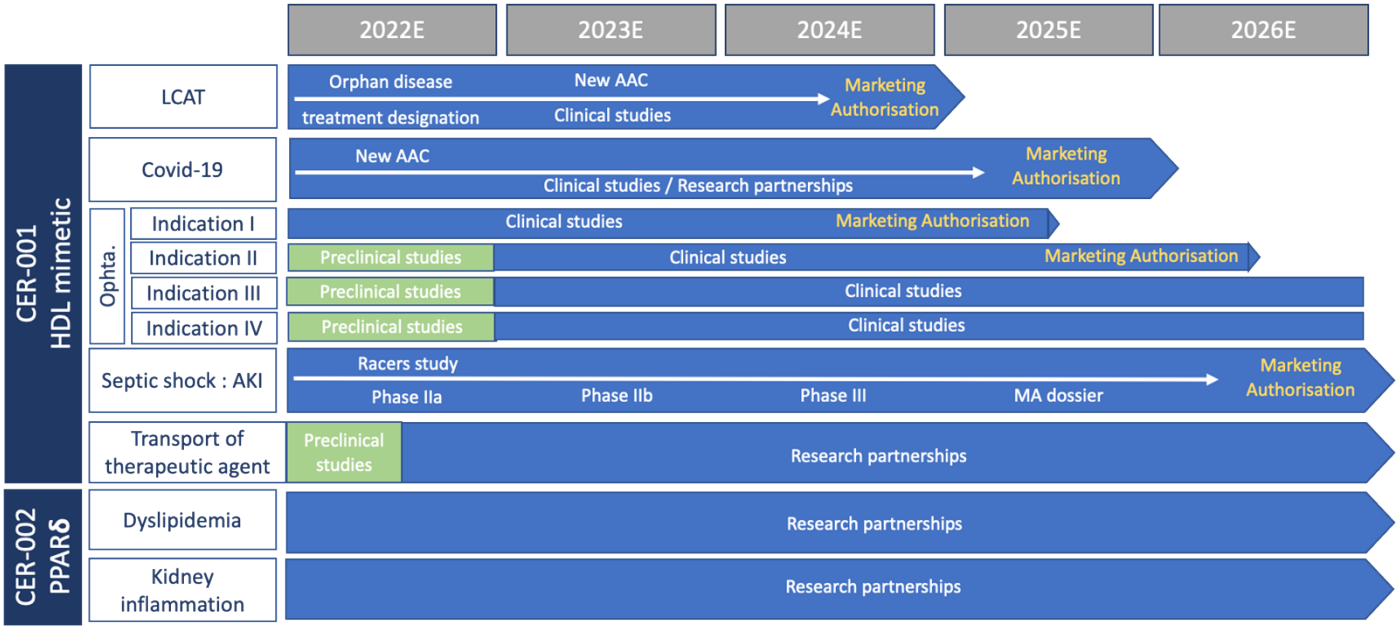
A growing pipeline with approaching market launches

Thanks to the orphan drug status obtained for LCAT deficiency, the first product launch could take place within two years. In the field of ophthalmology, thanks to Iris Pharma's know-how and the specificities linked to this speciality (reduced development times), according to us, the company should also be able to accelerate and market a first product by end-2024, followed by a rapid sequence of launches for the other targeted indicators.

In other areas, development is less advanced, which should prevent the company from launching a product in the marketing phase for several years (2025 for septic shock).

Finally, the company is working in other areas (e.g. AAC in the treatment of Covid-19) but it is still too early for them to be considered as part of the pipeline for at least the next 4-5 years.

Project pipeline forecast



Source: TPICAP Midcap

Short-term newsflow expected

Beyond the long-term outlook, we believe that 2022's short-term newsflow should remain strong, including:

- Phase IIa results for the Racers study (previewed for the autumn), and the launch of Phase IIb
- New UTAs/CTAs in the area of LCAT and the publication of associated results
- New UTAs/CTAs in Covid-19 and the publication of associated results
- Clarification of the priorities for targeted indicators in ophthalmology, study launches and some first results
- The probable determination of research lines for new indicators, notably in the form of partnerships for both the CER-001 molecule (as a transporter of active therapeutic agents, for example) and for the CER-002 molecule
- Publications that will integrate Iris Pharma into the group's operational perimeter (revenue and results in particular)

A landscape that will change with the integration of the Iris Pharma's business

Regarding the income statement presentation, as Iris Pharma is consolidated over 12 months in 2022, FY CRO revenue should increase to €6.5m (restated for intra-group). For the following years, we are integrating 3-5% growth/year for CRO revenue.

For the other activities we are forecasting:

- revenue from the LCAT gene mutation (a few hundred patients diagnosed in the US and Europe): €190k estimated for 2022, €1.1m for 2023 and €3.8m in 2024
- revenue from projects in the field of ophthalmology: we have included the launch of a first product at the end of 2024, which will generate the first revenue in this new therapeutic area (€500k estimated)

- no revenue from the septic shock study: given the consortium's funding of the Racers study, the company is contributing by providing CET-001 free of charge for patients included in the study. For the study's next phases, which will probably also be carried out in partnership, it is still too early to define the modalities, so we have not included any revenue from CER-001 for septic shock in our forecasts.
- no revenue from CAA or future Covid-19 studies. Again, the group will most likely have to rely on partnerships for this indicator, the terms and conditions of which are difficult to anticipate at this time.
- No revenue for other indicators where management aims to establish research programmes or technology licensing agreements. Revenue could be recorded quickly, however as at this stage no such agreements have been concluded, it is difficult to incorporate these elements into our modelling. Therefore, we have not forecast any revenue from these new indicators.

Overall, our 2022 revenue forecast stands at €6.7m, vs. €0.7m for 2021 reported, or €6.4m on a pro forma basis (including Iris Pharma's CRO activity net of intra-group revenue). In the following years, the company should benefit from the expected revenue from the development and commercialisation of the treatment for the orphan disease LCAT deficiency, and the start of sales in the ophthalmology segment.

Revenue forecasts by activity / indicator

M€	2020	2021	2021 pf	2022E	2023E	2024E
CRO	-	0,6	6,3	6,5	6,7	7,0
Chg	-	-	-	-	3,0%	5,0%
LCAT	-	0,03	0,03	0,19	1,1	3,8
Chg	-	-	-	-	x6,0	x3,4
Optha.	-	-	-	-	-	0,5
Chg	-	-	-	-	-	-
Others	-	-	-	-	-	-
Total sales	**0,0**	**0,68**	**6,4**	**6,7**	**7,8**	**11,3**
Chg	**-**	**Ns**	**Ns**	**Ns**	**17%**	**45%**

Source: TPICAP Midcap

Regarding the results, Iris Pharma's full-year consolidation, on one hand, and revenue generation from the LCAT and Ophthalmology indicators, on the other, will lead to a change in the face of the group's income statement, with the generation of a gross margin in particular.

In the CRO business, all expenses are included in the cost of goods sold, and the research tax credit will be recorded for R&D, leading the 2021 pro forma accounts to a relatively low gross margin/revenue ratio (less than 7% of revenue), and to a decrease in R&D expenses compared to the published accounts (€2.9m vs. €3.8m). In addition, in 2021, with a view to consolidating Iris Pharma in the Group's accounts (transition to IFRS), certain adjustments have been made, such as the revenue recognition method, the value of certain inventories and business provider agreements, which led to the recording of non-recurring expenses and thus impacted the results, resulting in a pro forma EBITDA of €6.7m compared with €5.8m in the published accounts.

In terms of gross margin, we have included a slight increase in the MB/revenue ratio for the iCRO business in the coming years (up to 9% by 2024 in our scenario), a gross margin of 75% for the LCAT indicator and 90% for the Ophthalmology indicator (treatment less concentrated in the CER001 molecule, see assumptions in the valuation section), leading to a positive mix effect on the level of MB/CA: almost 35% expected by 2024.

We also include an acceleration of R&D expenditure from 2022 onwards, notably for Ophthalmology projects and the new Covid-19 project, which will not be compensated during the period by revenues from the marketing of products. In the short term, the group's operating losses should therefore increase: -€7.8m expected for 2022 and losses at -€12.6m for 2023, then revenue growth should probably allow a reduction in losses from 2024 onwards.

Earnings forecasts

M€	2017	2018	2019	2020	2021	2021 pf	2022E	2023E	2024E
Sales	**0,0**	**0,2**	**0,0**	**0,0**	**0,7**	**6,4**	**6,7**	**7,8**	**11,3**
Cost of goods sold	-	-	-	-	-0,4	-5,9	-6,0	-6,4	-7,4
Gross Profit	**-**	**-**	**-**	**-**	**0,3**	**0,4**	**0,7**	**1,4**	**3,9**
% of sales	-	-	-	-	38,4%	6,8%	9,9%	18,5%	34,7%
G&A expenses	-1,2	-2,3	-1,8	-1,2	-2,2	-3,8	-4,0	-5,0	-5,5
R&D expenses CIR excl.	-4,9	-3,7	-0,7	-1,7	-3,8	-2,9	-4,0	-8,5	-10,0
EBITDA	**-6,1**	**-5,8**	**-2,5**	**-2,9**	**-5,8**	**-6,7**	**-7,3**	**-12,1**	**-11,6**
Depreciation and amortisation	-0,6	-1,4	0,0	0,0	-0,1	-	-0,5	-0,5	-0,5
EBIT	**-6,6**	**-7,2**	**-2,5**	**-3,0**	**-6,0**	**-**	**-7,8**	**-12,6**	**-12,1**
Financial result	1,7	0,7	4,4	1,2	0,1	-	0,0	0,0	0,0
NP	-5,0	-6,5	1,8	-1,9	-5,8	-	-8,2	-12,8	-12,4
Corrected NP*	-5,0	-5,0	-3,0	-3,1	-5,8	-	-8,2	-12,8	-12,4

* Corrigé des frais de réorganisation en 2019 et de l'abandon des créances BPI en 2019 et 2020

Source: TPICAP Midcap

Cash burn forecast

Given the financing of preclinical stages, research programmes (LCAT, ophta, kidney, etc.) and the relaunch of production of the CER-001 molecule (delivery in H1 2022, with new orders likely to come), even if some clinical studies could be carried out in partnership (e.g. the Racer study), and even if the company should continue to benefit from research tax credits (€1.8m in 2021), based on our current scenario, we estimate that the company will have a negative FCF in the order of €10-12m per annum in the coming years.

In view of the current financial situation, thanks to the fundraising completed at the end of 2021, we believe that the company has the means to finance its beginning-2022 development, which should enable it to use the results of the Racers Phase IIa study, or the presentation of the development strategy in Ophthalmology to raise funds once again and accelerate research in subsequent years.

Based on our revenue and operating expense assumptions, we estimate the company's financing needs to be around €25-30m over the next three years. Taking into account a financing only by capital increase (possible subsidies or external financing of research as for the Racers study), based on the current 2022 price and then on the price per share proposed at the time of the takeover of Iris Pharma (at €3.6/share, in our opinion, a minimum once the development strategy in Ophthalmology has been unveiled and the projects launched), this would lead to the creation of approximately 10.2m shares, 41% of the number of shares available at end-2021 (including the Iris Pharma target premium paid in shares in 2024).

Projected cashflow statement and change in net position

M€	2017	2018	2019	2020	2021	2022E	2023E	2024E
Cash flow	-8,2	-5,7	-2,6	-2,7	-4,9	-7,7	-12,3	-11,9
Capex	0,0	0,0	0,0	-0,1	-0,2	-0,1	-0,1	-0,1
Change in WCR	-0,9	-0,3	-1,3	2,1	-1,7	-1,2	-0,5	-0,2
FCF	**-9,1**	**-6,0**	**-4,0**	**-0,7**	**-6,9**	**-8,9**	**-12,9**	**-12,2**
Disposals	0,0	0,0	0,0	0,0	0,0	0,0	0,0	0,0
Financial invesments	-0,2	0,0	0,0	0,0	1,5	0,0	0,0	0,0
Dividends	0,0	0,0	0,0	0,0	0,0	0,0	0,0	0,0
Others	0,0	0,0	0,0	0,0	0,0	0,0	0,0	0,0
Cash excess (deficit)	**-9,3**	**-6,0**	**-4,0**	**-0,8**	**-5,4**	**-8,9**	**-12,9**	**-12,2**
Change in debt	0,8	0,0	-0,2	-0,2	0,0	0,0	0,0	0,0
Change in equity	0,2	1,2	1,0	1,8	4,0	5,0	12,0	12,0
Change in cash	-8,4	-4,8	-3,1	0,8	-1,4	-3,9	-0,9	-0,2
Cash available	16,3	11,5	8,3	9,2	7,9	4,0	3,1	2,9
Net cash	**10,0**	**6,0**	**7,1**	**9,1**	**3,0**	**-1,0**	**-1,9**	**-2,1**

Source: TPICAP Midcap

Valuation Methods

Valuation by target indicator

Although it is likely that the company will establish new research partnerships to advance the development of certain targeted indicators, and/or may license out its molecules, at this stage, we believe it is still too early to give value to such considerations. Therefore, we are basing our valuation approach on the areas where the company is most advanced, namely the use of CER-001 in patients with an LCAT gene mutation, in patients admitted to intensive care due to septic shock, and in the field of Ophthalmology (two indicators included in our valuation approach at this stage).

CER-001 and the LCAT gene mutation

The LCAT gene mutations are a rare to extremely rare pathology, only concerning about thirty families (Source: Montreal Heart Institute), with 215 cases described throughout the world (Europe, Japan and Canada for the vast majority). The prevalence of this orphan disease (no treatment available) is probably higher (less than 1/1,000,000 to date), but given the state of research in this field, screening is infrequent and announcements concerning new cases are poorly documented. Indeed, of the 25 queries received by the company since the publication of its research results, several patients were not listed.

The promising results obtained for the French and Italian patients, who were at advanced stages of kidney filtration capacity impairment, bode well for the molecule's efficacy for this type of disease. The aim is to offer the treatment to other patients, including those who are not yet at a stage that would require them to be put on dialysis in the short-term, so as to halt the process of deterioration of kidney functions as soon as possible, and the evolution of other pathologies probably linked to this mutation, such as corneal lipid deposits.

If we refer to the cost of treatments for certain orphan diseases, a series of CER-001 injections could cost several hundred thousand euros. In France, for example, among the latest treatments put on the market with this rare disease designation: Spinraza (Nusinersen, Biogen company), which concerns a serious muscular disorder (spinal muscular atrophy or SMA), has been reimbursed since September 2018: €88,300 for a single injection, which amounts to €530k for the first year of treatment, and €265k/year in subsequent years. For the same indicator, Zolgensma (Novartis), which obtained its Marketing Authorisation in 2019 and which at this time only requires one injection, costs €1.9m (marketing rate in the United States), becoming one of the most expensive treatments in the world. The cost of rare disease treatments is usually covered by healthcare systems (public or private) or by associations/foundations.

Even if the LCAT gene mutation concerns only a few patients worldwide (thus, a limited therapeutic target), given the potential cost of injections. The revenue generated by the treatment could be significant at the company level. More importantly, the development of such a treatment would undoubtedly highlight the novel field of action of the CER-001 molecule, which could facilitate/accelerate research partnerships for other indicators with higher prevalence.

According to the results of the first ATU, the molecule appears to be rapidly (treatment of less than 6 months) and durably (at one year) effective on patients at a very advanced stage of renal function deterioration. Additionally, high doses appear to be well tolerated (toxicity tests passed in phase III in previous studies but on lower dose protocols). We consider that the research work has a high probability of successfully completing phase II and III clinical trials.

To establish potential revenue from the commercialisation of CER-001 for the treatment of the LCAT gene mutation, we have based our model on several assumptions:

- Continuation of research on the basis of ATU/AAC and discussion with the authorities for marketing authorisation as a treatment for an orphan disease (reduced registration costs) and commercial launch at the end of 2024.
- The treatment's cost, at the time of marketing in 2024, will amount to €250k/patient for the first year of treatment (discount during the research phases, perhaps free of charge, by prudence no revenue integrated into our revenue forecasts for the group) and €125k/year for the following years of treatment.
- Partnership studies and external funding (subsidies in the context of an orphan disease) compensating for the operational costs linked to the research programmes.
- Twenty to thirty patients treated each year at cruising speed (more diagnosis worldwide and low risk of competing products due to the prevalence of the disease).

Flow chart for CER-001 forecast in LCAT

€m	2022	2023	2024	2025	2026	2027	2028
No. of new patients	**3**	**5**	**10**	**20**	**22**	**25**	**25**
Patients in treatment	3	6	10	19	37	56	75
Treatment price in first year (€000s)	*63*	*125*	*250*	*250*	*250*	*250*	*250*
Treatment price over following years (€000s)		*125*	*125*	*125*	*125*	*125*	*125*
Sales per year	0,2	1,1	3,8	7,4	10,2	13,2	15,6
Gross margin	0,2	0,8	2,9	5,6	7,6	9,9	11,7
% sales		*75,0%*	*75,0%*	*75,0%*	*75,0%*	*75,0%*	*75,0%*
Taxes					-0,8	-2,5	-3,9
FCF	**0,2**	**0,8**	**2,9**	**5,6**	**6,9**	**7,4**	**7,9**
Discounted FCF	**0,2**	**0,7**	**2,2**	**3,7**	**3,9**	**3,7**	**3,4**
Terminal value	59						
Discounted terminal value	22						
Sum of discounted FCFs	18						
WACC	15%						
Perpetual growth rate	1,5%						
Estimated value of LCAT treatment	**40**						

Source: TPICAP Midcap

The estimated value of the CER-001 molecule in the LCAT field, according to our model, is estimated at €40m.

CER-001 and septic shock

The term sepsis covers a broad spectrum of heterogeneous clinical presentations with variable prognosis but with common pathophysiological mechanisms. Sepsis is generally classified into three categories of increasing severity based on organ failure: sepsis, severe sepsis and septic shock.

A publication based on the collection of databases from several countries from 1979 to 2015 (Fleischmann C, JRespir Crit Care Med. 2015), and evidence from studies conducted in the field of sepsis, established an incidence of 288 cases of sepsis treated in hospitals per 100,000 people and an incidence of 148 for severe sepsis (including septic shock). The publication shows an increase in incidence over time (increase in the population at risk and better diagnosis). In the last ten years, 437/100,000 patients were treated for sepsis, and 270 for severe sepsis. In addition, during this period, the mortality rate observed in hospitals was 17% for sepsis and 26% for severe sepsis (even higher for septic shock). Data is not available from developing countries, so the global prevalence is difficult to precisely establish. But its extrapolation from the studied data points to an estimated at 31.5m patients treated worldwide for sepsis each year, and 19.4m for severe sepsis.

A Canadian study was conducted from July 1999 to March 2002, involving 4,845 patients admitted to intensive care with suspected sepsis (Kevin B, 2005, Intensive care Med). Of the total, 1,227 deaths were recorded over the follow-up period (683 days), representing 25% of patients. Of the 4,845 patients, 2,522 were classified as septic shock (over half). Of these 2,522 patients in septic shock, mortality totalled 31% (778 people), the vast majority of whom (640 people) died within 28 days of hospitalisation.

Despite significant advances in the understanding of the immuno-pathological mechanisms of sepsis, no therapeutic intervention has yet been effective, leading to an overall mortality of more than 30% in septic shock. These poor outcomes are often the result of failure to manage early with aggressive treatment (within 6 hours of suspected diagnosis). Once lactic acidosis and decompensated metabolic acidosis have set in, particularly in association with multi-visceral failure, septic shock is frequently irreversible and fatal. This is why patient prognosis for septic shock is often very poor within 48 hours of admission to the ICU.

Given the severity of septic shock and the occurrence of death at early stages, the effects of administering CER-001 to the patients included in the study were quickly measurable, making it possible to publish results on the first 10 patients as early as April 2022, even though the first patient was not included in the study until June 2021 and the Covid-19 health crisis slowed down the rate of inclusion of the following patients

The study also focuses on the response of the patients, depending on the dose of CER-001 they were given (determining the strong dose and comparing it to patients who did not receive the molecule).

Finally, the 28-day survival of the patients concerned could be an element of attention. However, with a cohort of only 20 patients, it is likely that no conclusions can be drawn on this criterion.

To establish the potential revenue for CER-001 in septic shock, we have based our model on several assumptions:

- Continuation of research: publication of Phase IIa results in autumn 2022 and launch of Phase IIb (80 to 120 people for a cohort, 200 to 250 in the case of several cohorts), and launch of Phase III in 2024 (cohort of 600 to 1,000 patients), regulatory steps for MA in 2025 and commercial launch in 2026.
- A treatment price of €10,000 per patient at the time of market launch in 2025 (discount during the research phases, possibly free of charge, conservatively no revenue included in our revenue forecasts for the group), compared to the cost of a patient in intensive care (several thousand euros per day).
- Based on a prevalence of 270 severe sepsis cases per 100,000 inhabitants, and based on the current population in North America and Europe, this represents a potential of over 3m patients per year. With 55,000 patients eventually targeted each year in our model, this represents less than 2% of severe sepsis in the areas concerned for a treatment of patients that could be a game changer in the field.
- Phase IIa financed by the Italian consortium. Cost of phase IIb estimated at €10m and cost of phase III at €30-40m (survival rate at 28 days allowing rapid results). As with Phase IIa, the company could set up partnerships and/or obtain external funding (grants and research tax credits), which is difficult to estimate at the moment, as are the terms of such partnerships, which are therefore not included in our model.

Forecast flow chart for CER-001 in the field of septic shock

€m	2022	2023	2024	2025	2026	2027	2028	2029
No. of patients	**20**	**100**	**500**	**500**	**5 000**	**25 000**	**35 000**	**55 000**
Treatment price (€000s)	*4*	*7,5*	*7,5*	*7,5*	*10,0*	*10,0*	*10,0*	*10,0*
Sales per year	0,1	0,8	3,8	3,8	50,0	250,0	350,0	550,0
Gross margin	0,1	0,5	2,6	2,6	35,0	175,0	245,0	385,0
% sales		*70,0%*	*70,0%*	*70,0%*	*70,0%*	*70,0%*	*70,0%*	*70,0%*
Operational costs				-0,5	-0,5	-0,5	-0,5	-0,5
R&D costs		-15,0	-15,0	-15,0	0,0	0,0	0,0	0,0
Taxes					-3,5	-17,5	-24,5	-38,5
FCF	**0,1**	**-14,5**	**-12,4**	**-12,9**	**31,1**	**157,1**	**220,1**	**346,1**
Discounted FCF	**0,1**	**-12,6**	**-9,4**	**-8,5**	**17,8**	**78,1**	**95,1**	**130,1**
Terminal value	2 602							
Discounted terminal value	851							
Sum of discounted FCFs	291							
WACC	15%							
Perpetual growth rate	1,5%							
Estimated value of Sepsis treatment	**1 141**							

Source: TPICAP Midcap

Based on our assumptions, the value of CER-001 in the field of septic shock amounts to €1,141m. Given the large number of patients admitted to intensive care each year for sepsis, the high mortality rate for severe sepsis, and the serious medical consequences for patients, particularly in terms of renal failure, the discovery of a molecule that could reduce the effects of sepsis shock and even improve survival rates has considerable potential, even under more conservative assumptions.

Sensitivity table of the CER-001 valuation in the field of septic shock

		No. of patients						
		25 000	**35 000**	**45 000**	**55 000**	**65 000**	**75 000**	**85 000**
Treatment price (€000s)	**2,5**	271	316	360	405	449	494	539
	5	383	472	561	650	740	829	918
	7,5	494	628	762	896	1 030	1 164	1 297
	10	606	784	963	**1 141**	1 320	1 498	1 677
	12,5	717	940	1 164	1 387	1 610	1 833	2 056
	15	829	1 097	1 364	1 632	1 900	2 168	2 436
	17,5	940	1 253	1 565	1 878	2 190	2 503	2 815
	20	1 052	1 409	1 766	2 123	2 480	2 837	3 194

Source: TPICAP Midcap

In ophthalmology

Although the prioritised indicators have not yet been announced, apart from uveitis, in view of the pathologies concerned by problems of lipid deposits (AMD, diabetic diseases, etc.), and existing treatments (imperfect because some have serious side effects), we believe that the population concerned by the treatments developed by the group could be very large, with rapid market penetration. However,

as a matter of caution, we have considered that if the group were to invest in four drugs for the ophthalmic segment in parallel (excluding combo drugs, i.e. those carrying other therapeutic agents), only two would lead to a commercial launch. To value these two indicators, we based our model on several assumptions:

- Research: overall cost of €10m per drug, borne over 4 years and financed entirely by the company, with marketing authorisation and commercial launch at the end of 2024 for product 1 (uveitis) and 2025 for product 2.
- A treatment price of €100 per patient from the moment uveitis is launched on the market and €600 per year per patient (treatment every two months for life) in the case of indicator 2.
- Rapid growth in patient numbers due to the combined effects of the molecule's efficacy, the size of the markets addressed, the relative price of the treatment, and Iris Pharma's market knowledge.
- A 90% MB/revenue ratio due to the low dose of CER-001 required for ophthalmia treatment.

Forecast flow chart for CER-001 in uveitis

€m	2022	2023	2024	2025	2026	2027	2028	2029
No. of patients	**0**	**0**	**5 000**	**50 000**	**250 000**	**750 000**	**1 500 000**	**3 000 000**
Treatment price (€000s)	*0*	*0*	*100*	*100*	*100*	*100*	*100*	*100*
Sales per year	0,0	0,0	0,5	5,0	25,0	75,0	150,0	300,0
Gross margin	0,0	0,0	0,5	4,5	22,5	67,5	135,0	270,0
% sales			*90,0%*	*90,0%*	*90,0%*	*90,0%*	*90,0%*	*90,0%*
Operational costs			-0,5	-0,5	-0,5	-0,5	-0,5	-0,5
R&D costs	-2,0	-5,0	-2,5	0,0	0,0	0,0	0,0	0,0
Taxes			0,3	-0,4	-2,2	-6,7	-13,5	-27,0
FCF	**-2,0**	**-5,0**	**-2,6**	**4,0**	**19,8**	**60,3**	**121,1**	**242,6**
Discounted FCF	**-2,0**	**-4,3**	**-1,9**	**2,6**	**11,3**	**30,0**	**52,3**	**91,2**
Terminal value	1 824							
Discounted terminal value	596							
Sum of discounted FCFs	179							
WACC	15%							
Perpetual growth rate	1,5%							
Estimated value of Sepsis treatment	**775**							

Source: TPICAP Midcap

Forecast flow chart for CER-001 in Ophthalmology (2)

€m	2022	2023	2024	2025	2026	2027	2028	2029	2030
No. of patients	**0**	**0**	**0**	**5 000**	**25 000**	**100 000**	**200 000**	**350 000**	**525 000**
Treatment price (€000s)	*0*	*0*	*0*	*600*	*600*	*600*	*600*	*600*	*600*
Sales per year	0,0	0,0	0,0	3,0	15,0	60,0	120,0	210,0	315,0
Gross margin	0,0	0,0	0,0	2,7	13,5	54,0	108,0	189,0	283,5
% sales			*90,0%*	*90,0%*	*90,0%*	*90,0%*	*90,0%*	*90,0%*	*90,0%*
Operational costs			-0,5	-0,5	-0,5	-0,5	-0,5	-0,5	-0,5
R&D costs	-0,5	-2,0	-5,0	-2,5	0,0	0,0	0,0	0,0	0,0
Taxes					-1,3	-5,4	-10,8	-18,9	-28,3
FCF	**-0,5**	**-2,0**	**-5,5**	**-0,3**	**11,7**	**48,2**	**96,8**	**169,7**	**254,7**
Discounted FCF	**-0,5**	**-1,7**	**-4,2**	**-0,2**	**6,7**	**23,9**	**41,8**	**63,8**	**83,3**
Terminal value	1 915								
Discounted terminal value	544								
Sum of discounted FCFs	213								
WACC	15%								
Perpetual growth rate	1,5%								
Estimated value of Sepsis treatment	**757**								

Source: TPICAP Midcap

The estimated value of drug 1 for ophthalmology is estimated to amount to €775m in the field of uveitis, and drug 2 amounting to €757m.

Stock market rating and price target

Given the initial results obtained in the field of LCAT, the absence of treatment for this rare disease, and the probable orphan disease status, we are confident in the company's ability to deploy CER-001 to this indicator. Therefore, we are not discounting the value obtained with our model (€40m).

In the field of severe sepsis, as the studies are less advanced (phase IIa in progress), we have chosen, as a matter of caution, to consider a significant discount to the valuation for this indicator in our valuation approach (95% discount, leading to a value of €57m).

For Ophthalmology, again as a matter of caution since the studies are in their preliminary phases, we apply significant discounts to the theoretical value obtained, but lower for sepsis, thanks to Iris Pharma's know-how, leading to an 85% discount for the uveitis indicator and 90% for indicator 2, for a valuation of €116m and €76m respectively, included in our valuation approach.

For the other targeted indicators (CER-001 as a transport agent for other therapeutic products, PPAR molecule, etc.), for the time being, their current stages of development do not allow us to establish a valuation, thus we have not included them in our approach (zero value retained).

We have estimated that the future fundraising and the premium on Iris Pharma's objective: paid in shares in 2024, would be based on a share price of €3.6, except for 2022, where we have taken the current share price as a basis, leading to a number of listed shares of 36.1m at the end of 2024, a number of shares that serves as a reference for our estimate of the current value per share of the group, which constitutes our price objective.

Summary of our valuation approach

	NPV (M€)	Discount	Value (M€)
CER-001 : LCAT	40	0%	40
CER-001 : Severe sepsis	1 141	95%	57
CER-001 : Ophthalmology 1	775	85%	116
CER-001 : Ophthalmology 2	757	90%	76
CER-001 : Ophthalmology others	0	-	-
CER-001 : Transport of therapeutic agent	0	-	-
PPAR : Dyslipidemia	0	-	-
PPAR : Kidney inflammation	0	-	-
EV for projects under developpement (M€)			289
Net debt at end 2021 (M€)			(3,0)
Provisions (M€)			0,5
			292
Current nb of shares			27,9
No. of shares after bonus shares and excl. treasury stock			29,6
Diluted value per share (€)			9,9
Estimated fund raising over 3 years			29,0
No. of shares after fund raising			39,8
Value per share (€)			**8,1**

Source: TPICAP Midcap

Our price target is €8.1/share, which offers a potential upside of more than 400% compared to the current price.

The change in ownership and management, the repositioning of research programmes, the first published results, and the merger with Iris Pharma (paid for in shares based on a value of €3.6/share in December 2021) have enabled the stock to rise over the past few years: x2.9 in 2019, x2.5 in 2020 and x2.5 in 2021. However, since the beginning of 2022, the share price has fallen by 35%, which we believe is linked to the current economic and geopolitical environment, as the company's newsflow has remained buoyant. We believe that this decline in the share price provides a strong entry point for the stock, which is likely to resume its upward trajectory, thus reinforcing our Buy rating.

Annexes: Research Fields

HDL

Definition

Cholesterol is a fatty substance produced by the liver and certain foods that plays an important role in the body. It is involved in the secretion of hormones. There are two main types of cholesterol transporters: HDL (High Density Lipoproteins) and LDL (Low Density Lipoproteins) lipoproteins, which are known as the strong and the bad cholesterol respectively.

The most studied role of HDL is its capacity to ensure the return transport of cholesterol, i.e. to promote the efflux of cellular cholesterol, the transport of cholesterol in the blood and its delivery to the liver for recycling, in other words its capacity to participate in the elimination of fats by the organism, hence the qualification of "good cholesterol".

HDL are natural endogenous nanoparticles that transport multiple hydrophobic biological molecules in an aqueous medium (blood), such as lipids like cholesterol, triglycerides and phospholipids, but also vitamins, hormones, proteins, nucleic acids as well as elements foreign to the organism like drugs. Among these proteins, apolipoproteins are elements specific to the different classes of lipoproteins. Thus, apolipoprotein A-I (apoA-I) is essentially present in HDL and plays a role both in structuring the HDL nanoparticle and as an intermediary with other partners, either cellular (interaction with receptors or cellular transporters) or enzymatic (such as Lecithin-Cholesterol AcylTransferase).

The fields of action of HDL are therefore diverse, which opens the way to potential indicators that go well beyond cardiovascular diseases (the main field of research of Cerenis Therapeutics until 2018).

Fields of Action

It is well known that low HDL levels are a major risk factor for cardiovascular disease. It has been shown that HDL plays a role in preventing the formation of atherosclerotic plaques in the artery walls. Atherosclerosis is a cardiovascular disease that corresponds to a thickening of the arterial wall due to hypercholesterolemia (literally high cholesterol) by the deposition of a plaque consisting mainly of lipids and cells, which can lead to a progressive narrowing of the internal diameter of the artery. This causes the passage of oxygenated blood to the organ being supplied to be impeded. This results in angina pain if a coronary artery is affected, but can lead to severe heart problems or strokes.

Most of the studies that are being conducted in the field of HDL mimetics are therefore focused on cardiovascular disease, and this is the choice that has been made historically by Cerenis Therapeutics' management teams.

New studies tend to show the role of lipoproteins in other pathologies, for example in brain function. It is increasingly recognised that abnormalities in brain lipid metabolism are closely linked to the pathogenesis of major neurodegenerative diseases such as Alzheimer's disease and vascular dementia.

Other studies have helped to highlight the broad fields of action of HDL with anti-inflammatory and antioxidant functions. Moreover, while all lipoproteins (HDL and LDL) bind lipopolysaccharides (molecules considered toxic and which induce fever, septic shock, a decrease in blood pressure, etc. in humans) allowing an increase in bacterial clearance, only HDL ensures their neutralisation.

A study conducted on patients admitted to intensive care for septic shock or sepsis (Tanaka et al. Annals of Intensive Care, January 2021) tends to prove, for example, that lipoproteins decrease during sepsis, and demonstrates the major role of HDL in the survival of septic patients treated in intensive care: correlation between the decrease in HDL levels during the first three days and the survival of patients.

Although the importance of the presence of HDL in the human body no longer needs to be demonstrated, the synthesis of the molecule and its large-scale production remain very complex to this day.

Control of bioproduction

To enable the development of potential treatments based on or in combination with HDL, the first step is the production of a synthetic lipoprotein (stability of formulation, no risk of cross-transmission, etc.) that mimics as closely as possible the structure and functions of a natural high density lipoprotein (HDL).

Abionyx has overcome significant historical difficulties in manufacturing such an HDL particle and has developed a proprietary process. This process incorporates the three key steps required to manufacture a functional HDL mimetic:

1. The production of pure human apoA-I

In Abionyx's manufacturing process, apoA-I is expressed as pro-apoA-I, a natural precursor that allows the secretion of the mature apoA-I protein into the culture medium, making it easier to collect the protein and requiring fewer purification steps afterwards.

Using a genetic engineering technology to which it holds exclusive rights (agreement with Catalent, which co-developed the product, 1% royalties on future revenues), Abionyx has created a mammalian cell strain integrating the human apoA-I gene, which expresses and secretes it. This unique and innovative strain is owned by the company. During culture, the cells multiply and secrete human apoA-I into the culture medium (the supernatant). Over time, this medium becomes enriched with recombinant human apoA-I, without the need to break the cells to extract the apoA-I, thus avoiding contamination of the apoA-I by the cell's own proteins. The cell culture conditions were successfully optimised as the scale was scaled up from 10 litres to 1000 litres.

2. Optimisation of the composition of the particle's phospholipids:

Abionyx has optimised the phospholipid composition by incorporating selected phospholipids based on the composition and electrical charge of natural HDL. Natural HDL particles are composed of apoA-I and phospholipids, some of which are neutral and others negatively charged, which gives them their biological properties and prevents the particles from being degraded and eliminated too quickly by the kidneys.

Sphingomyelin is a characteristic phospholipid of natural HDL. Sphingomyelin has a higher affinity for cholesterol than lecithin, and contributes to the release of cellular cholesterol by providing a medium within the HDL particle that facilitates its capture. Abionyx has also developed an innovative patent-pending process for the synthesis of sphingomyelin.

Other HDL mimetics have been manufactured primarily with lecithin, an uncharged lipid from egg yolk or soybeans, which differs significantly from the charged mixture of phospholipids found in natural HDL particles (i.e. neutral and charged phospholipids). Abionyx is, to its knowledge, the only company with a patent covering negatively charged lipoprotein complexes.

3. The assembly to create a homogeneous population of stable discoidal particles:

The manufacturing process developed by Abionyx to assemble the discs is patented. It takes advantage of the temperature-dependent behaviour of phospholipids to combine apoA-I and phospholipid naturally, to spontaneously create a homogeneous and stable population of charged discoidal (disc-shaped) HDL particles. This process can be easily scaled up for commercial production using commonly used manufacturing equipment.

The molecule developed by the company, named CER-001, is thus a complex comprising the natural human HDL protein apolipoprotein A-I (apoA-I) and phospholipids, the composition of which has been optimised to obtain a negatively charged discoidal nanoparticle resembling a native HDL particle. The production of the molecule is outsourced to two partners (contracts established in 2021 when the production of the molecule is re-launched to meet the demand of the research programmes).

PPARs

PPARs (Peroxisome Proliferator Activated Receptors) are nuclear receptors on cells that are activated by the binding of certain fatty acids or lipids. They describe a group of proteins in a cell that work together to help control the expression of certain genes and the use of lipids (fats) and glucose (sugar) in the body.

PPARs were discovered in 1990. Their roles in the regulation of many metabolisms, and in particular lipid metabolism, are of biological and clinical interest because of the therapeutic prospects associated with them. Three major PPAR isotopes, encoded by different genes, have been identified: PPAR (alpha), PPAR (gamma) and PPAR / (beta or delta). PPAR and PPAR have been identified as therapeutic targets for Hypertriglyceridaemia and insulin resistance, respectively.

PPAR/ is a potential pharmacological target for the treatment of disorders associated with the metabolic syndrome. Metabolic syndrome is not a disease per se, but rather the presence of a set of physiological signs that increase the risk of type 2 diabetes, heart disease or stroke. Other indicators for PPARs are currently being investigated:

- NASH/NAFLD (Non-Alcoholic Steato-Hepatitis / Non-Alcoholic Fatty Liver Disease)
- Acute Kidney Injury (AKI)
- Primary Biliary Cholangitis (PBC): a chronic liver disease in which the immune system attacks the liver causing damage to the bile ducts

- Mitochondrial diseases, PMM or Primary Mitochondrial Myopathy: genetically induced disorders that lead to oxidative phosphorylation defects affecting mainly skeletal muscle i.e. muscles under voluntary control of the central nervous system (blood vessels, nerves, sensory organs, common connective tissue, and muscle cells), but not only
- Systemic lupus erythematosus: an autoimmune disease attacking the body's connective tissue, present throughout the body: skin, eyes, tendons, muscles, organs, etc.
- Fatty Acid Oxidation Disorder (FAOD): absence or deficiency of the enzymes necessary for the breakdown of lipids, resulting in delayed mental and physical development.

While PPARs molecules were discovered many years ago, the research launched for new indicators, and the first promising results of the latter, have revived interest in these classes of molecules, including for big pharma. For example, Astellas finalised the acquisition of Mitobridge at the end of 2017-beginning of 2018 (a research partnership from which the ASP-1128 programme presented above was derived). The Japanese company exercised the option (signed before the launch of a phase I trial in Duchenne muscular dystrophy in 2013) it held on the capital of Mitobridge, valuing the structure at $225m in total, to which may be added an additional price that may not exceed $225m (depending on the results of clinical developments).

Under a licensing agreement with Nippon Chemiphar Co. established in 2005, the company selected from a catalogue a molecule that enabled it to develop a highly selective PPARδ agonist named CER-002 (Phase I clinical trial completed), which allows the management to restart work on this molecule. A policy of patent rejuvenation has also been launched with, in particular, the acquisition of a patent in September 2020 on several families of PPAR.

FINANCIAL DATA

Income Statement	12/19	12/20	12/21	12/22e	12/23e	12/24e
Sales	0.0	0.0	0.7	6.7	7.8	11.3
Changes (%)	-100.0	na	na	890.7	16.9	44.9
Gross profit	0.0	0.0	0.3	0.7	1.4	3.9
% of Sales	na	na	38.4	9.9	18.5	34.7
EBITDA	**-2.5**	**-2.9**	**-5.8**	**-7.3**	**-12.1**	**-11.6**
% of Sales	na	na	-864.1	-109.7	-154.1	-102.1
Current operating profit	**-2.5**	**-3.0**	**-6.0**	**-7.8**	**-12.6**	**-12.1**
% of Sales	na	na	-881.8	-117.2	-160.5	-106.5
Non-recurring items	0.0	0.0	0.0	0.0	0.0	0.0
EBIT	-2.5	-3.0	-6.0	-7.8	-12.6	-12.1
Net financial result	4.4	1.2	0.1	-0.0	-0.0	-0.0
Income Tax	-0.0	-0.1	0.0	-0.3	-0.2	-0.3
Tax rate (%)	2.0	-6.4	0.0	-3.7	-1.9	-2.1
Net profit, group share	**1.8**	**-1.9**	**-5.8**	**-8.2**	**-12.8**	**-12.4**
EPS	0.08	na	na	na	na	na

Financial Statement	12/19	12/20	12/21	12/22e	12/23e	12/24e
Goodwill	0.0	0.0	5.4	5.4	5.4	5.4
Tangible and intangible assets	0.0	0.1	0.4	0.3	0.2	0.1
Right of Use	0.0	0.0	0.0	0.0	0.0	0.0
Financial assets	0.1	0.1	3.0	2.7	2.4	2.1
Working capital	0.5	-1.8	0.3	1.5	2.0	2.2
Other Assets	0.0	0.0	0.0	0.0	0.0	0.0
Assets	0.5	-1.5	9.1	9.9	10.0	9.8
Shareholders equity group	6.7	6.6	10.7	7.5	6.7	6.3
Minorities	0.0	0.0	0.0	0.0	0.0	0.0
LT & ST provisions and others	1.0	1.0	1.4	1.4	1.4	1.4
Net debt	-7.1	-9.1	-3.0	1.0	1.9	2.1
Other liabilities	0.0	0.0	0.0	0.0	0.0	0.0
Liabilities	0.5	-1.5	9.1	9.9	10.0	9.8
Net debt excl. IFRS 16	-7.1	-9.1	-3.0	1.0	1.9	2.1
Gearing net	-1.1	-1.4	-0.3	0.1	0.3	0.3
Leverage	2.8	3.1	0.5	-0.1	-0.2	-0.2

Cash flow statement	12/19	12/20	12/21	12/22e	12/23e	12/24e
CF after elimination of net borrowing costs and taxes	1.7	-1.6	-4.8	-8.0	-12.6	-12.2
ΔWCR	-1.3	2.1	-1.7	-1.2	-0.5	-0.2
Operating cash flow	0.4	0.5	-6.6	-9.2	-13.1	-12.4
Net capex	0.0	-0.1	-0.2	-0.1	-0.1	-0.1
FCF	-4.0	-0.7	-6.9	-8.9	-12.9	-12.2
Acquisitions/Disposals of subsidiaries	0.0	-0.1	-0.2	-0.1	-0.1	-0.1
Other investments	0.0	0.0	1.5	0.0	0.0	0.0
Change in borrowings	-0.2	-0.2	-0.0	0.0	0.0	0.0
Dividends paid	0.0	0.0	0.0	0.0	0.0	0.0
Repayment of leasing debt	0.0	0.0	0.0	0.0	0.0	0.0
Others	1.0	1.8	4.0	5.0	12.0	12.0
Changes in exchange rates	0.0	0.0	0.0	0.0	0.0	0.0
Change in net cash over the year	-3.1	0.8	-1.4	-3.9	-0.9	-0.2
ROE (%)	27.7%	na	na	na	na	na
ROCE (%)	na	209.2%	na	na	na	na

DISCLAIMER

Analyst certifications

This research report (the “Report”) has been approved by Midcap, a business division of TP ICAP (Europe) SA (“Midcap”), an Investment Services Provider authorised and regulated by the Autorité de Contrôle Prudentiel et de Résolution ("ACPR"). By issuing this Report, each Midcap analyst and associate whose name appears within this Report hereby certifies that (i) the recommendations and opinions expressed in the Report accurately reflect the research analyst’s and associate’s personal views about any and all of the subject securities or issuers discussed herein and (ii) no part of the research analyst's or associate’s compensation was, is or will be directly or indirectly related to the specific recommendations or views expressed by the research analyst or associate in the Report.

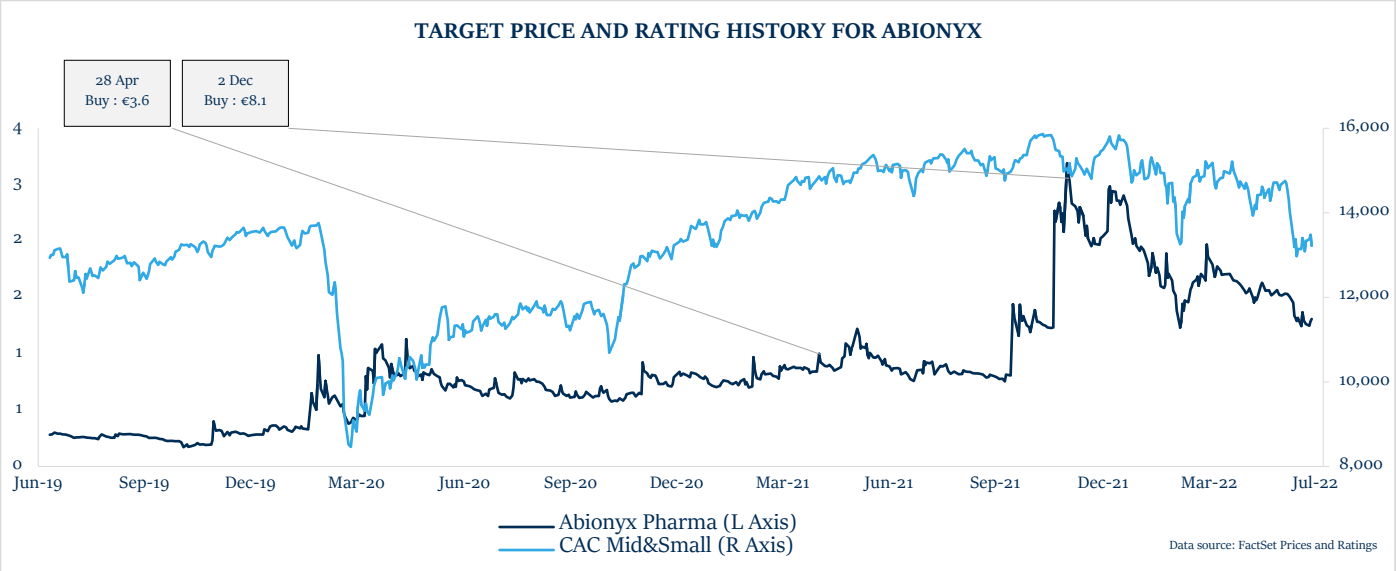
Methodology

This Report may mention evaluation methods defined as follows:
1. DCF method: discounting of future cash flows generated by the company's operations. Cash flows are determined by the analyst's financial forecasts and models. The discount rate used corresponds to the weighted average cost of capital, which is defined as the weighted average cost of the company's debt and the theoretical cost of its equity as estimated by the analyst.
2. Comparable method: application of market valuation multiples or those observed in recent transactions. These multiples can be used as references and applied to the company's financial aggregates to deduce its valuation. The sample is selected by the analyst based on the characteristics of the company (size, growth, profitability, etc.). The analyst may also apply a premium/discount depending on his perception of the company's characteristics.
3. Assets and liabilities method: estimate of the value of equity capital based on revalued assets adjusted for the value of the debt.
4. Discounted dividend method: discounting of estimated future dividend flows. The discount rate used is generally the cost of capital.
5. Sum of the parts: this method consists of estimating the various activities of a company using the most appropriate valuation method for each of them, then realizing the sum of the parts.

Conflict of Interests

D. Midcap or any related legal entity is a market maker or liquidity provider with whom a liquidity agreement has been entered into in respect of the Issuer's financial instruments: Abionyx Pharma
G. Midcap and the Issuer have agreed to the provision by the former to the latter of a service for the production and distribution of the investment recommendation on the said Issuer: Abionyx Pharma

History of investment rating and target price – Abionyx Pharma



Distribution of Investment Ratings

Rating	Recommendation Universe*	Portion of these provided with investment banking services**
Buy	86%	93%
Hold	12%	7%
Sell	2%	0%
Under review	0%	0%

Midcap employs a rating system based on the following:
Buy: Expected to outperform the markets by 10% or more over a 6 to 12 months horizon.
Hold: expected performance between -10% and +10% compared to the market over a 6 to 12 months horizon.
Sell: Stock is expected underperform the markets by 10% or more over a 6 to 12 months horizon.

The history of ratings and target prices for the Issuers covered in this report are available on request at marketing@midcapp.com.

General Disclaimer

This Report is published for information purposes only and does not constitute a solicitation or an offer to buy or sell any of the securities mentioned herein. The information contained in this Report has been obtained from sources believed to be reliable, Midcap makes no representation as to its accuracy or completeness. The reference prices used in this Report are closing prices. All opinions expressed in this Report reflect our judgement at the date of the documents and are subject to change without notice. The securities discussed in this Report may not be suitable for all investors and are not intended to recommend specific securities, financial instruments, or strategies to particular clients. Investors should make their own investment decisions based on their financial situation and investment objectives. The value of the income from your investment may vary due to changes in interest rates, changes in the financial and operating conditions of companies and other factors. Investors should be aware that the market price of the securities discussed in this Report may be volatile. Due to the risk and volatility of the industry, the company, and the market in general, at the current price of the securities, our investment rating may not correspond to the stated price target. Additional information regarding the securities mentioned in this Report is available on request.

This Report is not intended for distribution or use by any entity who is a citizen or resident of, or an entity located in any locality, territory, state, country, or other jurisdiction where such distribution, publication, availability, or use would be contrary to or limited by law or regulation. Entity or entities in possession of this Report must inform themselves about and comply with any such restrictions, including MIFID II. Midcap has adopted effective administrative and organizational arrangements, including "information barriers", to prevent and avoid conflicts of interest regarding investment recommendations. The remuneration of financial analysts who participate in the preparation of the recommendation is not linked to the corporate finance activity.

Notice to US Investors:

This Report was prepared, approved, published, and distributed by Midcap, a business division of TP ICAP (Europe) SA (“Midcap”), a company located outside of the United States. This Report is intended for distribution only to major U.S. institutional investors (as defined in Rule 15a-6 under the U.S. Securities Exchange Act of 1934 (the “Exchange Act”)) pursuant to the exemption in Rule 15a-6 and any transaction effected by a U.S. customer in the securities described in this Report must be affected through Louis Capital Markets, LLC (“LCM”) and not with or through Midcap. Midcap is not registered as a broker-dealer under the Exchange Act. Midcap is not a member of the Financial Industry Regulatory Authority, Inc. (“FINRA”), SIPC, or any other U.S. self-regulatory organization.

Midcap is the employer of the research analyst(s) responsible for this Report. The research analysts preparing this Report are residents outside the United States and are not associated with LCM or any US regulated broker-dealer. The analyst(s) is/are not subject to supervision by a US broker-dealer and are not required to satisfy the regulatory licensing requirements of FINRA or required to otherwise comply with US rules or regulations regarding, among other things, communications with a subject company, public appearances and trading securities held by a research analyst account.

Analyst Certification. Each of the analysts identified in this Report certifies, with respect to the companies or securities that the individual analyses, that (1) the views expressed in this Report reflect his or her entity’s views about all of the subject companies and securities and such recommendations were elaborated independently; and (2) no part of his or her compensation was, is or will be directly or indirectly dependent on the specific recommendations or views expressed in this Report. This material was produced solely for information purposes and for the use of the recipient. This Report does not constitute an offer of, or an invitation to buy or sell any security.

The information contained herein has been obtained from published information and other sources which are considered to be reliable. The companies noted herein accept no liability or responsibility whatsoever for the accuracy or completeness of any such information. All estimates, expressions of opinion and other subjective judgments contained herein are made as of the date of this document. Midcap, or its affiliates, has not managed or co-managed a public offering of securities for the subject company in the past 12 months, has not received compensation for investment banking services from the subject company in the past 12 months, does not expect to receive and does not intend to seek compensation for investment banking services from the subject company in the next 3 months. Midcap, or its affiliates, do not beneficially own 1% or more of the subject securities and there are not any other actual, material conflicts of interest noted at the time of the publication of this research report. As of the publication of this Report, Midcap does not make a market in the subject securities. Midcap will refrain from initiating follow-up contacts with any recipient of this

Report that does not qualify as a Major Institutional Investor or seek to otherwise induce or attempt to induce the purchase or sale of any security addressed in this Report by such recipient.