# LETTER TO OUR SHAREHOLDERS



Vector of innovation.



#### **CONTENTS**

MESSAGE FROM CHAIRMAN - p3
SHARE PRICE EVOLUTION UNCORRELATED WITH
ONCODESIGN'S ECONOMIC & TECHNOLOGICAL PROGRESS - p4
IDDS: A NEW SERVICE OFFERING - p6
2019 INVESTOR DAY - p10

POINT OF VIEW OF VÉRONIQUE FOUTEL - p11 LATEST NEWS - p12 BROKERS' RATING - p14 AGENDA & KEY FIGURES - p15 ONCODESIGN AT A GLANCE - p16

#### MESSAGE FROM THE CHAIRMAN

Philippe Genne, Chairman and CEO



We are still in the real Darwinian world in which you don't have to be a clairvoyant to see that the health sector is in great need of innovations, & will continue to be for a long time yet.

#### Modern day pharaohs

The pharaohs' main objective was to work to ensure eternal life through enormous monuments into which they sank their fortune and the blood of their people. We could compare the heads of some major Silicon Valley companies to modern day pharaohs seeking eternal life for themselves; according to them, death is the last big illness to overcome and, thanks to artificial intelligence, this goal is getting closer... there is thus a great battle underway in the high tech and GAFA microcosm driven by the megalomania of some bosses seeking deification.

Life is therefore no longer biological but computational, and intelligence is no longer adaptation but artificial.

The world of finance, always keen on certain fleeting pleasures, has understood this; there is scope to speculate and create bubbles. Yet again, their playful and opportunistic side is leading them to confuse the means and the ends. But diseases are still among us and are very physiological, affecting millions of living and breathing human beings who belong to a Humanity that still only has its intelligence to improve and create more treatments, and thus survive. We are still in the real Darwinian world in which you don't have to be a clairvoyant to see that the health sector is in great need of innovations, and will continue to be for a long time yet. We are patiently creating tomorrow's companies that will outlive today's pharaohs.

Oncodesign has reported a health appraisal that has been positively received by the analysts and journalists that follow the Company, with a substantial 42% increase in service revenue in 2018, the signing of a major partnership with Servier laboratories consecrating the therapeutic research undertaken within its walls, and the prospect of a drug candidate by the end of the year. Its only problem is a Euronext Growth stock market valuation that appears to have leveled off at €50 million. Investors no longer believe in biotechnologies in France, and are instead massively investing in the construction of AI pyramids in Las Vegas.

It's weird to observe that, during the bank holidays, of which there are a number in May, the continual low number of shares traded in this sector does not vary; only bots are working. Maybe robots have already replaced financiers; the AI revolution began through them in the shadows, and it seems they may be taking over.

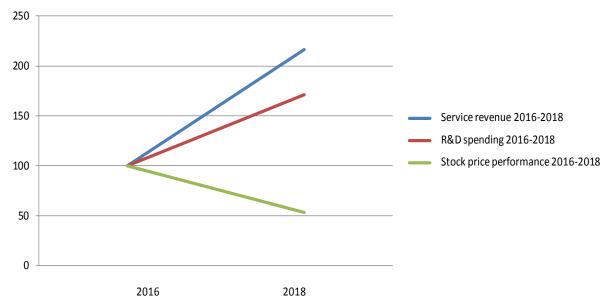
For those of you who are still with us at this point of the editorial and follow the Company closely, Oncodesign is facing the challenge of diversified industrial development, and in the coming months we will address strategic issues to ensure the rapid growth and subsequent creation of value that you are all awaiting. This will require substantial work, but it is nothing we cannot do and we will put all the energy we need into it.

Best regards to you all. I look forward to seeing you at the Shareholders' Meeting of June 20.

Philippe Genne

# SHARE PRICE EVOLUTION UNCORRELATED WITH ONCODESIGN'S ECONOMIC & TECHNOLOGICAL PROGRESS

Over the last three years, Oncodesign has more than doubled its service revenue and increased its R&D efforts by over 70% without burning cash or calling on the markets.

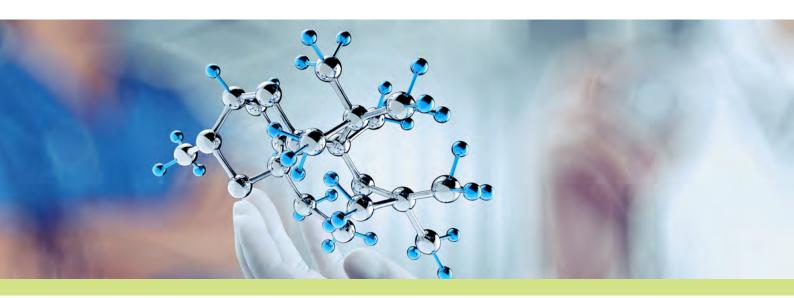


Source: Oncodesign 2019

The evolution of the Company's share price does not reflect Oncodesign's economic and technological progress, but a market severely affected by the outflow of capital that is particularly penalizing the biotech sector and small caps. The index comprising small cap biotechs has thus fallen by close to 75% over the last two years, this phenomenon also having been accentuated by robots and algorithms that fail to take into account companies' fundamentals. We remain particularly confident in our Group's development potential, which is perfectly illustrated by the major partnership we have just signed with the Servier group. The latter concerns €320 million in milestones excluding royalties, or almost 4 times what we had previously negotiated with Ipsen (€80 million) regarding the same research program.

Furthermore, given our technological investments, Oncodesign's addressable market is now worth €14.5 billion, compared with €0.5 billion in 2016.

Within this context, given our valuation that is stuck at €50 million, the Company is looking at various non-dilutive solutions to develop its employee shareholding in order to involve as many staff as possible in the Group's rapid development.





### Integrated Drug Discovery Services (IDDS)

# A new service offering aimed at biopharmaceutical & pharmaceutical companies

#### THE PERMANENTLY (RE)EVOLVING BIG PHARMA BUSINESS MODEL!

Over the last 25 years, the global pharmaceutical industry has undergone a profound change that has led to structural, geographical and specialty changes and the expansion or discovery of new markets. Between 1995 and 2005, the blockbuster period (Lipitor®, Plavix®, Nexium®, etc.) was marked by a wave of mergers and acquisitions that had a twofold objective: maintain a profitability margin through economies of scale, but also diversify the portfolio and activities via various therapeutic fields. The purpose is to offset the forecast loss of numerous patents for flagship molecules, but also to control the severe lack of R&D productivity for new molecules. Indeed, as most general medicine illnesses have already found therapeutic answers, there were fewer and fewer easy solutions. There were many such mergers, Astra and Zeneca, Sanofi and Aventis, Glaxo and Smithkline to mention but three, which led to the formation of massive research entities, multiple production sites, the juxtaposition of sales teams and the creation of multi-layered governance making the integration of newly-formed entities difficult. Unfortunately, this "Bigger is Better" approach was a disaster for R&D, as reflected by the number of new products approved each year by the FDA at the end of this period (2005, 2006 and 2007).

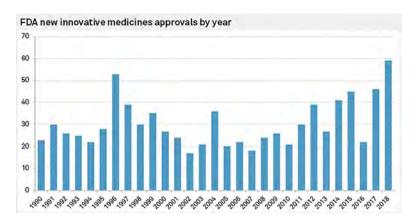


Figure 1: New treatments approved per year by FDA (Food and Drug Administration). Source : S&P Global Market Intelligence 2019

As the entire R&D development cycle for a new product is around ten years, this trend had been anticipated by the pharmaceutical industry. Since 2005, major pharmaceutical companies have altered their model and offers from general medicine to specialized medicine or rare diseases, while simultaneously focusing in-house research on their traditional therapeutic fields. This strategy of moving towards specialty medicine, via the use of small molecules or biological molecules, was notably made possible by:

- the acquisition of highly-specialized biotechnology companies (Roche and Genentech or Sanofi and Genzyme);
- the migration of large research centers to scientific centers of excellence where academic and private labs rub shoulders (Boston, San Diego, Cambridge, Shanghai). This transition also led to a reduction in the size of the teams, the aim being to introduce a more flexible and agile biotech-type entrepreneurial model;
- the outsourcing of some research activities to innovative services companies via strategic discovery partnerships. This growth in the outsourcing of research activities revitalized a directly related sector of activity: Drug Discovery services companies.

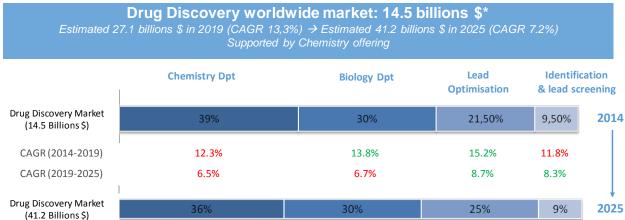
In 2018, 59 new active substances were approved by the FDA, a record high in terms of filings and a 37% increase compared with 2017, which had already been a good year. Is the tactic adopted by pharmaceutical labs to seek innovation through an organized network of partners and service providers beginning to bear fruit?

#### DRUG DISCOVERY SERVICES COMPANIES ARE BOOMING!

The Drug Discovery Services company story began in the 1940s, with the setting up of Huntingdon Life Sciences (UK) and Charles Rivers Laboratories (US). Pulled along by pharmaceutical labs for the first few decades, they gradually restructured themselves to cope with the cost pressures induced by pharmaceutical laboratories' falling returns on R&D investment:

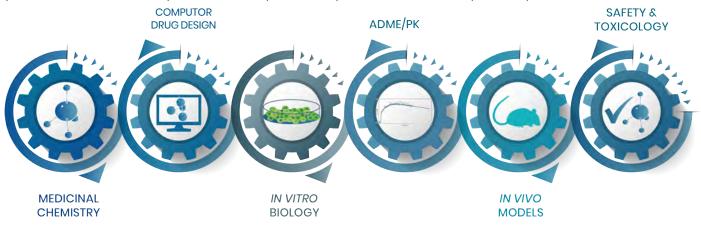
- Their traditional fee-for-service business model had to adapt in order to ensure excellence and reduce R&D costs. In the 2010s, this economic mutation led to the implementation of more flexible service alliances, with premiums paid when the Drug Discovery services provided exceed expectations, but also strategic partnerships between Drug Discovery services companies and pharmaceutical laboratories with part of the risk of failure borne by the services company via payments based on success.
- Drug Discovery services companies' expertise has been substantially enhanced by expertise from former pharmaceutical research sites. Thanks to this new mindset, services companies now have the ability to design and manage a research program in an environment that meets pharmaceutical laboratories' R&D standards.

Multiple restructuring has considerably increased the maturity of Drug Discovery services companies by encouraging the emergence of players who are capable of undertaking comprehensive new drug discovery programs: Evotec, Charles River, Wuxi and, more recently, Oncodesign. The range of services now covers the identification and validation of molecular targets, the design and characterization of molecules that can interact with these targets through to the wide-scale synthesis and regulatory toxicology stages. A VisionGain study published in 2015 estimated the size of the Drug Discovery services companies' market at USD 14.5 billion with annual growth of 7.2% a year through to 2025.



#### ONCODESIGN'S NEW POSITIONING ON THE INTEGRATED DRUG DISCOVERY SERVICES MARKET

For almost a quarter of a century, Oncodesign has been providing in vivo and in vitro pharmacological services to pharmaceutical and biotechnology companies in the field of oncology, immuno-oncology, inflammation, autoimmune disorders and infectious diseases. Over €200 million has been invested in the construction of a precision medicine technological platform, a real driving force for Oncodesign clients' innovation. The search for new drug candidates, before the clinical evaluation phases, is a lengthy and complex process involving a range of highly-qualified specific professions and areas of expertise where experience in pharmaceutical development is pivotal.



<sup>3 -</sup> Based on Global Data report (2018), updated and enriched by the company

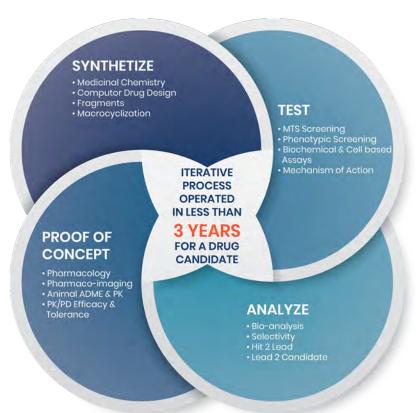


Figure 4: Iterative Process to deliver a drug candidate in less than 3 years.

Oncodesign, over time and thanks to its various acquisitions (François Hyafil research center in 2016, Bertin Pharma's teams in 2017), is now able to provide a highly comprehensive Integrated Drug Discovery Service (IDDS) offering.

Each member of staff has their own personality and each partner has different requirements, but Oncodesign's experience and the values we share with our clients enable us to speak the same language.

Together, we draw up a coherent strategy and development plan. The integration of different specialties on a same research platform offers our clients a number of advantages:

- a single experienced contact manages the entire project, facilitating communication and proximity;
- permanent overview of the entire process and the progress achieved;
- significant time saved by not having to manage a number of service providers;
- free-flowing exchange of data between platforms enabling the panel of experts to make quick & enlightened decisions.

Over almost 25 years, Oncodesign has developed a service culture based on innovation, quality and speed. Our close ties to the pharmaceutical industry and the experience of our staff give us the discipline and inventiveness required to solve complex scientific issues. Today, we make all of our expertise and abilities available to our clients to enable them to move their research projects forward, to the benefit of patients.

# November 2018 - Signature of a partnership agreement with Galderma laboratory



- Multi-annual service contract
- Focuses mainly on designing & discovering new drug candidates in dermatology

#### Sources.

Brother in arms, Dr John Montana, Drug Discovery World Summer 2015
VisionGain, Drug Discovery Outsourcing Market Forecast 2015-2025, 2015
Contract Research Organizations Are Seeking Transformation in the Pharmaceutical Value Chain, ACS Med. Chem. Lett. 2019, 10, 684–686
Biotech & Finances n°855, May 13, 2019



#### **EVENT: A LOOK BACK AT THE 2019 INVESTOR DAY**

### LRRK2 KINASE INHIBITORS FOR TREATING PARKINSON'S DISEASE: AN ONCODESIGN STRATEGIC PROGRAM



Oncodesign held its 2019 Investor Day on March 12, providing it with an opportunity to talk about its LRRK2 program, which targets Parkinson's disease, and the signing of a strategic partnership agreement with Servier in this indication



Philippe Genne Founder, CEO - Oncodesign



Jan Hoflack CSO - Oncodesign

### Oncodesign's LRRK2 inhibitors have unique potential to modify Parkinson's disease

There is solid evidence linking LRRK2 to Parkinson's: LRRK2 mutations represent the highest identified risk of declaring the familial form of this disease. A high level of LRRK2 activity is also observed in idiopathic patients. In recent years, the pharmaceutical industry has thus developed substantial interest in LRRK2 kinase inhibitors.

#### Oncodesign's LRRK2 program in partnership with Servier Laboratories

Further to the signing of a strategic cooperation agreement between Oncodesign and Servier to develop LRRK2 kinase inhibitors in Parkinson's disease, Christophe Thurieau, Director of Server Research Centers, discussed the LRRK2 kinase's potential in Parkinson's for Servier and the importance of this partnership.

Christophe Thurieau explained his partnership policy, and in particular the reasons for choosing Oncodesign:

- 1. An extremely selective proprietary platform
- 2. Numerous promising chemical leads



Christophe Thurieau Director Research Centers - Servier



Lastly, Véronique Foutel explained the Market Access challenges for a drug with a particular focus on Parkinson's disease.

Read the "Viewpoint of Véronique Foutel" article on page 11.

Dr. Véronique Foutel Founder & Managing Partner, Value Vision Consulting

Focus on the strategic collaboration between Oncodesign & Servier to develop LRRK2 kinase inhibitors in Parkinson's disease



- Servier has an option to exclusively license one or several drug candidates as soon as they are approved to enter Phase I.
- Servier will fund the entire program.
- Oncodesign will receive an upfront payment of €3 million at the signing of the partnership,
   & could receive up to €320 million, excluding royalties on sales.

### POINT OF VIEW OF DR. VÉRONIQUE FOUTEL

4

Dr. Véronique FOUTEL talks about the Market Access¹ challenges associated with the development of a drug, notably in Parkinson's disease.

# What are the challenges associated with the development of a new drug?

A new product is not synonymous with innovation, nor is it necessarily more useful than what already exists. In the biopharmaceutical domain, a new product — to be perceived as a genuine innovation and be financially covered at a justified price — must meet the three following criteria:

- enable the treatment or prevention of a pathology that represents a real health issue because of its severity or its impact on the population,
- be significantly more efficient and/ or tolerated than existing products, if possible by attacking the cause of the illness and altering the way it evolves,
- be accompanied by a low margin of uncertainty regarding the transposition of its clinical trial results into real-life performance.

As soon as the idea to design a new drug is born, or some 15 years before its launch on the market, these elements have to be taken into account and anticipated. Even if they cannot be reasonably substantiated by scientific proof, which is obtained fairly late on in the development process, they must be the main focus of R&D efforts.

Taking these considerations onboard, what can we say about the LRRK2 kinase inhibitors that aim to provide an in-depth treatment for Parkinson's disease & whose marketing is expected by the end of the decade?

Currently, Parkinson's disease – whose prevalence is increasing due to the aging population – does not benefit from any substantive treatment. By altering the cognitive and functional abilities of those affected by



Founder & Managing Partner, Value Vision Consulting

this illness through neuronal loss, sufferers graduate from disability to death. Indeed by 2030, this disease is likely to be one of the top 20 causes of death worldwide, according to the WHO. Recent breakthroughs regarding the natural history of this illness have helped us understand that it is an infliction that develops silently over decades before becoming symptomatic in the prodromal then motor stage. The first scientific elements resulting from preclinical studies and a Phase Ib clinical trial on LRRK2 inhibitors suggest that these drug candidates could not only delay the worsening of the disease's symptoms, but potentially delay the appearance of these symptoms.

### Can these LRRK2 kinase inhibitors be classified as potential medicinal innovations?

Should this neuroprotection potential be met for this severe neurodegenerative illness that has no therapeutic solution and weighs so heavily on society, the qualification of therapeutic innovation to representatives of this class would have to apply.

Indeed, nursing staff, patients and careers would at last have a major therapeutic weapon enabling them to fight dependence, delay institutionalization and maintain the quality of life of patients and careers alike. Such drugs would have to be approved for marketing.

# Please, find the Investor Day video on our website





<sup>1</sup> Process through which a biotechnology / pharmaceutical company ensures the accessibility and reimbursement of its product in as many countries as possible

<sup>2</sup> WHO Worldwide death projections 2016 –2030

#### LATEST NEWS



#### BIOTECH FINANCES - MARCH 12, 2019

#### Parkinson's: Servier signs a key R&D deal with Oncodesign

To identify a drug candidate that is efficient against Parkinson's within the coming three years, on Monday evening Oncodesign announced that it had signed a strategic R&D cooperation agreement with Servier Laboratories, a longstanding partner of the Group.

"This agreement today represents one of the biggest every signed in this domain by a French biotech at drug candidate research stage", says Philippe GENNE, CEO & founder of Oncodesign.



#### Oncodesign and Servier join forces to fight Parkinson's disease

In greater detail, Oncodesign will receive a €3 million upfront payment when the contract is signed and an additional €3 million a year to finance its research activities. "With some twenty dedicated researchers, this is equivalent to the Group's rate of spending last year", says the Midcap Partners firm. [...]

"The Group is again lending credibility to the solidity of its derisked and self-financed development model since its IPO in 2014, as well as its 2020 objectives, i.e. revenue of €40 million and a net profit", Midcap Partners continues.

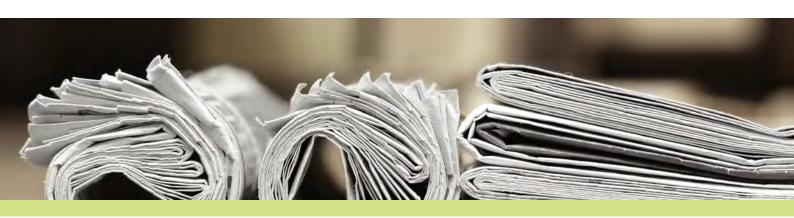


#### BFM Bourse - Tuesday March 12, 2019

#### An agreement with Servier in Parkinson's disease boosts Oncodesign's share price

For the first time in years, Oncodesign has seen a double-digit increase in its share price. The biotech, which specializes in the discovery of new drug candidates for major laboratories, has signed an immediately income-generating partnership agreement with Servier to develop a potential treatment for Parkinson's disease. [...]

"Today, the pharmaceutical industry is showing substantial interest in identifying new treatments for Parkinson's, notably regarding the LRRK2 kinase that is seen to be a high-potential target for treating this illness. Within the framework of this early-stage research agreement, Servier's expertise will be a real asset for undertaking this program that could lead, in the medium term, to the development of innovative drug candidates", said Philippe Genne, founder & CEO of Oncodesign.



### LATEST NEWS (continued)



#### LE QUOTIDIEN DU PHARMACIEN - MONDAY MARCH 18, 2019

#### Parkinson's disease: new kinase inhibitors offer a promising lead

Unlike the inhibitors currently available on the market, Oncodesign is developing a new generation of highly-targeted inhibitors, limiting side effects. Its technology enables the development of very specific and highly selective small macrocyclic molecules to inhibit the kinase responsible for this disease. [...]

On March 11, 2019, Servier and Oncodesign announced a strategic R&D cooperation agreement concerning one of more potential drug candidates to treat this illness. At this stage of development, the molecules show good oral bioavailability; they pass through the blood-brain barrier and act on the brain without any side effects at effective doses. A drug candidate is anticipated by 2020.

#### Usine Nouvelle - Tuesday March 12, 2019

#### Servier and Oncodesign are targeting the progression of Parkinson's disease

Currently, the only drugs available for Parkinson's merely treat the symptoms of this disease, say Servier and Oncodesign. Their aim is now to act in a different way to fight its evolution and stop the disease progressing.

The two French laboratories have thus just entered into a research and development cooperation agreement that could lead to one or more drug candidates for treating Parkinson's disease.

Within this framework, Servier is prepared to invest up to €320 million, having agreed to finance the entire program. What it stands to gain in the future is an option to exclusively license drugs resulting from this collaboration worldwide. Oncodesign, a Dijon-based biopharmaceutical laboratory, will undertake the research activities through to the selection of preclinical candidates, i.e. prior to the clinical trial phases.

#### ACTU LABO - WEDNESDAY APRIL 3, 2019

#### Servier and Oncodesign tackling Parkinson's together

"Conclusive data has established a link between LRRK2 hyperactivity and Parkinson's disease", explains Jan Hoflack, Oncodesign's Chief Scientific and Operating Officer. "LRRK2 inhibitors have the potential to act directly on this disease's progression."

"It is therefore a potential innovative in-depth treatment, when current treatments only aim to alleviate the symptoms of this illness", points out Philippe GENNE, founder & CEO of Oncodesign.

# Please find all investor news on our website







#### **BROKERS' RATING**



Broker	Analyst	Date	Recommendation
LOUIS CAPITAL MARKETS	Gilbert Ferrand	April, 12, 2019	Buy
Kepler Cheuvreux	Thomas Guillot	March, 12, 2019	Buy
CM-CIC Market Solutions	Fanny Meindre	April, 12, 2019	N/A
Bryan, Garnier & Co	Gary Waanders	March, 18, 2019	Buy



## News: OncoSNIPE® welcomes 2 New clinical partners

- Oncodesign's OncoSNIPE® program, initiated in 2017 and devoted to identifying and characterizing resistance to anti-cancer therapies, is welcoming two new partners: the Institut Curie and the Centre Léon Bérard. Professor Nicolas Girard's teams in Paris and Doctor Olivier Trédan's teams in Lyon will enable patient enrollment in the longitudinal clinical trial, which should include 600 patients by 2021, to be accelerated.
- OncoSNIPE® concentrates the research and development work of 10 industrial partners (Experts System, Acobiom, Sword, Oncodesign) and academic partners (Institut Paoli Calmettes, Centre Georges François Leclerc, Centre Hospitalier Universitaire de Strasbourg, henceforth joined by the Institut Curie and the Centre Léon Bérard) on 3 cancerous indications representative of the mechanisms of resistance and sensitivity to treatment: breast, pancreatic and lung cancer. The €12 million budget is supported by BPIFrance within the framework of the Investments for the Future program.
- Based on the implementation of bio-IT approaches combining artificial intelligence, statistical learning and semantic enrichment, OncoSNIPE® is designed to identify and characterize patients who are resistant to anti-cancer treatments. Its purpose is to guide the therapist when caring for a patient, or the pharmaceutical laboratory when developing new drugs, in order to ultimately reduce the rate of therapeutic failure.

# THE NOTEBOOK OF SHAREHOLDER



#### ONCODESIGN & THE STOCK MARKET

Euronext Growth Paris				
ISIN Code	FR0011766229			
Number of shares	6,818,412			
Market capitalization	42 M€*			
Share price	6,10 €*			
12 month high/low	10,7 € /6,34 €			

\*Data at June, 13, 2019





### ONCODESIGN CAPITAL STRUCTURE at December 31, 2018



#### 2019 CALENDAR



#### **Publication of FY 2019 Revenues:**

July 25, 2019 (after stock market closing)

#### **Scientific conferences**

- Anglo-Nordic Medicinal Chemistry Symposium, Snekkersten, June 11-14
- Bioheterocycles 2019 XVIII International Conference on Heterocycles in Bioorganic Chemistry, Ghent, June 17-20
- WPW World Pharma Week, Boston, June 17-20
- SNMMI Annual Meeting, Anaheim, June 22-25
- RICT 2019 Interfacing Chemical Biology and Drug Discovery - 55th International Conference on Medicinal Chemistry, Nantes, July 3-5

#### **DOCUMENTATION**



Our 2018 annual financial report is available in the Investor section of our website:





Flash this QRCode to access the investor section.

# A TEAM ATTENTIVE TO OUR SHAREHOLDERS



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#### AT ONCODESIGN, WE TAKE THE PRIVACY OF YOUR PERSONAL DATA VERY SERIOUSLY

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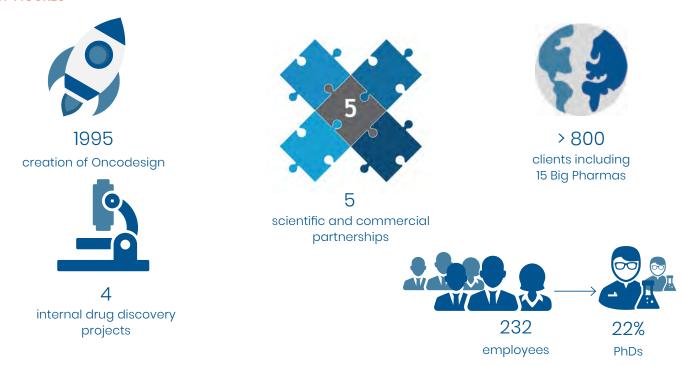
In line with the French Data Protection Act of January 6, 1978 as amended, you have a right to access and amend the data held concerning you.

You can access the information we hold about you by contacting us at oncodesign@newcap.eu CNIL reference 2102182 v 0.

#### **ONCODESIGN AT A GLANCE**

Oncodesign, a vector of innovation, is a biopharma company whose mission is to find new avenues of treatment using precision medicine based on its unique patient-centered innovation model.

#### **K**EY FIGURES



#### **OUR MISSION AND OUR TECHNOLOGICAL STRENGTH**

"Discover innovative new therapies effective against cancer and serious illnesses with unmet medical needs." Philippe Genne - Oncodesign Chairman & CEO.

Oncodesign's specific strength lies in its technology continuum, which covers the entire molecule discovery cycle from identification of resistant patient populations right through to the drug candidate. Oncodesign puts the patient at the heart of its technology continuum to target the problem of inherent or acquired therapeutic resistance. This innovation model sets us apart.



It is based on our three strategic activities:

- 1- Etiology of diseases
- 2- Discovery of new therapeutic target/ molecule combinations
- 3- Experimentation of new treatments.

#### **O**UR BUSINESS MODEL

Oncodesign leverages its strategic activities through three types of contractual arrangement:



#### **SERVICE**

Based on targets or molecules, Oncodesign provides services to other companies in selecting the best drug candidates.

Service revenue expected to reach €25-30 million in 2020



#### **PARTNERSHIP**

Programs to develop kinase inhibitors using our proprietary Nanocyclix® technology, and core technological partnerships.

Transition to phase III then commercial launch of the first radiotracer: AMM 2020-2021



#### **LICENSING**

Licensing of Oncodesign portfolio technologies, drug candidates and radiotracers.

A therapeutic composite in clinical trial by the end of 2020

- Signature of Integrated Drug Discovery Service (IDDS) contracts
- Signature of service partnerships
- External growth potential
- Development of other radiotracers
- Ramp-up and milestone payments for BMS and UCB
- Signature of new early-stage partnerships based on Nanocyclix® technology
- Development of OncoSNIPE® & IMODI technologies
- Build-up of a mature pipeline of kinase inhibitor drug candidates in oncology
- Selection of drug candidates (e.g.: LRRK2, RIPK2, ALK1 and MNK1/2)
- Signature of clinical development partnerships

#### What is a kinase inhibitor?

A kindse is a protein that speeds up chemical reactions in the body. Kinase deregulation is the cause of more than 400 diseases. This deregulation can be resolved by binding a small molecule to the kinase to block its activity.

#### What is a radiotracer?

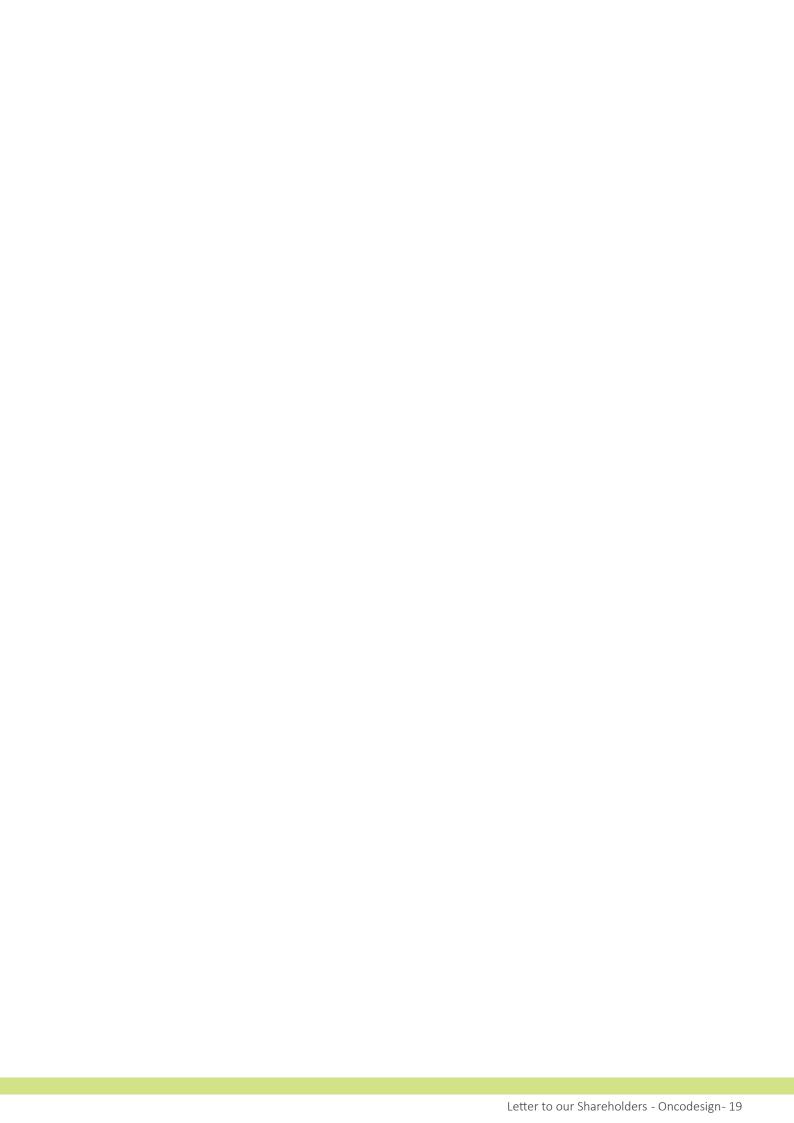
A traceable radioactive isotope added to a substance and used in imaging techniques such as Positron Emission Tomography (PET) to trace the path of the substance in an organ.

#### What is a biomarker?

A biomarker is an accurately measurable indicator of a particular bodily function, disease or action of a drug.



### **NOTES**



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