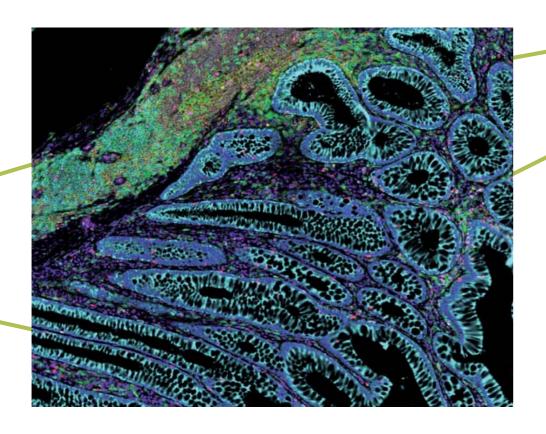




INNATE PHARMA S.A. IS A CLINICAL-STAGE BIOTECHNOLOGY COMPANY WITH A FOCUS ON DISCOVERING AND DEVELOPING FIRST-IN-CLASS THERAPEUTIC ANTIBODIES THAT HARNESS THE INNATE IMMUNE SYSTEM TO IMPROVE CANCER TREATMENT AND CLINICAL OUTCOMES FOR PATIENTS.

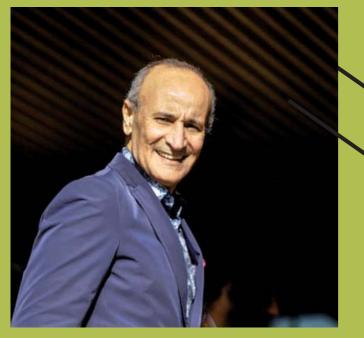


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## THE CHAIRMEN'S EDITORIAL





MONDHER MAHIOUR

HERVÉ BRAILLY

## **CONTINUING THE INNATE PHARMA JOURNEY**

MONDHER MAHJOUBI, CHAIRMAN OF THE EXECUTIVE BOARD SINCE JANUARY 2017 AND HERVÉ BRAILLY, CO-FOUNDER AND CHAIRMAN OF THE EXECUTIVE BOARD SINCE THE CREATION OF THE COMPANY, NOW CHAIRMAN OF THE SUPERVISORY BOARD, SHARE WITH US THEIR VISION OF INNATE PHARMA AND THE COMPANY'S FUTURE.

"THIS FIRST EVIDENCE

OF EFFICACY IS BOTH A MAJOR

STEP FOR INNATE PHARMA

AND A MESSAGE OF HOPE

TO PATIENTS"

### HERVÉ BRAILLY, WHAT SHOULD WE REMEMBER ABOUT 2016?

Firstly, in 2016 we obtained the first report of potential clinical benefit both for lirilumab, licensed to Bristol-Myers Squibb, and for IPH4102, our wholly-owned program. This is the maturation of the scientific approach that we

had envisioned 17 years ago. This first evidence of efficacy is both a major step for Innate Pharma and a message of hope to patients.

In parallel, we continue to build on our research work to ensure the relay of our portfolio: IPH4301, a first-in-class antibody with wide therapeutic potential, entered IND-enabling studies and we

initiated two new programs, IPH52 and IPH53, in the very promising field of tumor microenvironment.

We also continued our structuring in line with the development strategy of our business model towards the commercialization of our products: the teams were

strengthened by the recruitment of 30 new members of staff and we welcomed Mondher Mahjoubi who takes over from me at the head of the Executive Board.

## MONDHER MAHJOUBI, WHAT CONVINCED YOU ABOUT THE INNATE PHARMA PROJECT?

I had the opportunity to know and learn about Innate Pharma at the time of the agreement signed with AstraZeneca in 2015 for the co-development and commercialization of monalizumab and I was already impressed by the quality of work and the teams' expertise.

The Company's focus on oncology, a field that is close to my heart and that I know well, its specialization in immunotherapy and the know-how it has been able to develop around innate immunity were paramount in my decision to join Innate Pharma. The entrepreneurship and

the commitment of the teams were equally decisive. Finally the project to become an international biopharmaceutical company matches the type of entrepreneurial challenge that I was looking for after having spent over 25 years in the pharmaceutical industry fighting cancer and contributing to improving the lives of patients.

Furthermore, the Company has laid solid foundations

Furthermore, the Company has laid solid foundations with three molecules in clinical development, alliances with world famous industrial partners, a rich preclinical portfolio and innovative antibody technologies.

## HERVÉ BRAILLY, WHY DID YOU CHOOSE TO HAND OVER NOW AND TO MONDHER MAHJOUBI?

When we created Innate Pharma in 1999, it really was a scientific belief that we have turned into a portfolio of drug candidates.

Innate Pharma is entering a new phase of its development, that must now integrate late stage clinical activities and the preparation of the commercialization of its molecules. We can be proud of the progress accomplished and we want to enter the next stages with the confidence and determination required to have the best chance of success. Mondher Mahjoubi has vast experience in the commercial development of pharmaceutical products and in-depth knowledge of oncology issues in general and immuno-oncology in particular.

His human qualities and leadership convinced the entire Supervisory Board and he has all the skills necessary to lead the Company in the late stage development and the commercialization of its products.



Our goal is to become a fully-integrated biopharmaceutical company marketing our own products and I am convinced that Innate Pharma has all the "ingredients" to become a global leader in immuno-oncology.

We have been pioneers in the field of innate immunity and have developed scientific and technological know-how that has allowed us to discover and bring three innovative molecules to clinical development. We must continue to invest in research to enrich our portfolio and strengthen our scientific leadership in the field of immuno-oncology but we also have to evolve our business model and think patient first, become a company dedicated to the development and the commercialization of therapeutic solutions that contribute to improving and prolonging the life of patients with cancer.

As consequence we need to progress the clinical development of our products and deliver their full potential both for our partnered and proprietary programs, lirilumab and monalizumab, IPH4102 respectively.



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"INNATE PHARMA

HAS ALL THE "INGREDIENTS"

TO BECOME A GLOBAL LEADER

IN IMMUNO-ONCOLOGY"

IPH4102, which is being developed in cutaneous T-cell lymphoma, will be our first opportunity to give shape to this vision. To do this, we will progressively integrate new skills and expertise in the fields of late-stage clinical development, medical affairs, pharmacoeconomics, strategic marketing and commercialization.

Immuno-oncology is a fast growing and evolving field, in particular since the initial success of checkpoint inhibitors targeting PD-I/PD-LI, yet we are only at the beginning of a long journey that, I am convinced, will lead in the long-term to the control and cure of cancer. Meanwhile, immuno-oncology will

continue to develop with notably the identification of new biomarkers and the emergence of new combinations of molecules targeting different immune pathways. To play a part in this paradigm shift, we must be innovative and propose first-in-class molecules that can be combined with checkpoint inhibitors targeting PD-I/PD-LI whilst being well tolerated. Becoming a partner of choice in the combination strategies of immuno-oncology world leaders will be one of our priorities.

## MONDHER MAHJOUBI, WHAT ARE THE CHALLENGES FACING INNATE PHARMA IN ORDER TO ACHIEVE ITS AMBITIOUS OBJECTIVES?

Innate Pharma has assets that we must preserve: innovative research, highly committed teams, a strong culture of collective progress and a high degree of flexibility. The

recruitment and rapid integration of new skills as well as the retention of our talented employees should build on these assets.

At the same time, we are changing dimension, we need to adapt our organization and our decision-making processes, and manage internal balances in order to

integrate the late stage development and commercialization of our products.

We have to be prepared. Becoming a world-ranking commercial biotech does not come easily. I am highly confident in the ability of the teams at Innate Pharma to rise up to this challenge, individually and collectively. The Company has always been able to plan for the long-term and take measured risks. The work has got off to a good start so far and we will continue in this endeavor.

## **EXECUTIVE COMMITTEE**



MONDHER MAHJOUBI, MD CHAIRMAN OF THE EXECUTIVE BOARD

Appointed Chief Executive Officer and Chairman of the Executive Board on December 30, 2016, Mondher Mahjoubi was previously in charge of Oncology Strategy at AstraZeneca. His career has encompassed a number of positions at Roche-Genentech, Mayne Pharma, Sanofi-Aventis and Rhône-Poulenc Rorer. Dr Mahjoubi holds an MD, is an oncologist and a member of the American Society of Clinical Oncology and the European Society of Medical Oncology.



YANNIS MOREL, PHD
EXECUTIVE VICE PRESIDENT, CHIEF
BUSINESS OFFICER AND MEMBER OF
THE EXECUTIVE BOARD

Yannis Morel joined Innate Pharma in 2001 following his studies at the Ecole Normale Supérieure and a PhD in oncology. He held several R&D positions at Innate, initially as a scientist in the

immunology team before becoming team manager, then taking responsibility for research programs. In 2007, he became Head of Business Development. He particularly contributed to setting up the industrial partnerships with Bristol-Myers Squibb and AstraZeneca.



PIERRE DODION, MD, MBA
EXECUTIVE VICE PRESIDENT AND
CHIEF MEDICAL OFFICER

Pierre Dodion joined Innate Pharma in 2014. Medical Affairs Director at Pfizer, Novartis or Aventis, he contributed to the development, approval and launch of several drugs. He was Chief

Medical Officer then SVP Corporate Development and Operations at the American biotech ARIAD Pharmaceuticals, leading expansion operations in Europe. He is a medical doctor specialized in oncology, he also holds an MBA degree.



NICOLAI WAGTMANN, PHD EXECUTIVE VICE PRESIDENT, CHIEF SCIENTIFIC OFFICER AND MEMBER OF THE EXECUTIVE BOARD

Nicolai Wagtmann joined Innate Pharma in 2013, after having spent 14 years in the R&D division at Novo Nordisk A/S, where he built a portfolio of firstin-class therapeutic antibodies

for treatment of cancer and chronic inflammatory diseases. PhD in Immunology, he also held academic appointments at the National Institutes of Health and at the CIML (Center of Immunology in Marseille-Luminy).



LAURE-HÉLÈNE MERCIER, MBA EXECUTIVE VICE PRESIDENT AND CHIEF FINANCIAL OFFICER

Laure-Hélène Mercier joined Innate Pharma in 2007. Holder of an MSc in Neurosciences and an MBA degree, she began her career as an equity analyst at Oddo Securities and Natexis

Bleichroeder, prior to becoming Director of Investor Relations at Innate Pharma, contributing to the development of international shareholding and different fund raising by the Company. She was appointed Chief Financial Officer on December 30, 2016.



MARCEL ROZENCWEIG, MD EXECUTIVE VICE PRESIDENT AND PRESIDENT OF INNATE PHARMA INC

Dr. Rozencweig joined Innate Pharma in 2009. He is recognized as a world leading expert and opinion leader in medical oncology and anti-cancer drug development. He built and led the

clinical research group that developed all the NCEs brought by Bristol-Myers Squibb to the market from 1983 to 2001 in the area of cancer. Dr. Rozencweig is an Adjunct Associate Professor of Medicine at New York University, NY.



JÉRÔME TIOLLIER, PHD

EXECUTIVE VICE PRESIDENT AND CHIEF
DEVELOPMENT OFFICER

Jérôme Tiollier joined Innate Pharma in 2001. He spent 15 years working at the Pasteur Mérieux group, notably as Director of preclinical development then Director of Research and

Development Europe, contributing to the development of several drugs. He holds a PhD in cellular biology and immunology.

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# FOUNDATIONS TO BECOME A FULLY-INTEGRATED BIOPHARMACEUTICAL COMPANY

CREATING VALUE FOR EVERY STAKEHOLDERS: PATIENTS, STAFF, SHAREHOLDERS, INDUSTRIAL AND ACADEMIC PARTNERS, LOCAL ENVIRONMENT

MAJOR INDUSTRIAL PARTNERS

CLINICAL PROGRAMS

PRECLINICAL PROPRIETARY PIPELINE





€ 230.7 M

CASH
AND CASH
EQUIVALENTS

## DIFFERENTIATED SCIENCE IN IMMUNO-ONCOLOGY (IO)

- Pioneered the discovery and development of NK cells checkpoint inhibitors
- A new track in IO and IO combination therapies

## PARTNERSHIPS WITH LEADING IMMUNO-ONCOLOGY COMPANIES TO ACCELERATE OUR DEVELOPMENT

- Capacities allowing to maximize the potential of partnered products and to finance the proprietary assets of the Company
- Retained co-development / commercialization rights aligned with the financial, organizational and human capacities of the Company

## INTEGRATING PROGRESSIVELY EVERY STAGE OF THE VALUE CHAIN

- An active preclinical research to broaden the portfolio of proprietary products
- A portfolio of late-stage clinical products, of which two are partnerized
- Progressively integrating complementary skills to move toward commercial stage

"THE RESULTS ACCRUED THROUGHOUT 2016 WITH LIRILUMAB AND IPH4102 **ALLOW US TO CONSIDER AN ACCELERATION** IN THE DEVELOPMENT OF OUR MOST **ADVANCED PROGRAMS.**"

PIERRE DODION, EXECUTIVE VICE PRESIDENT, CHIEF MEDICAL OFFICER

## **3 CLINICAL PROGRAMS**

Lirilumab

LICENSED TO BRISTOL-MYERS SQUIBB

ANTIBODY POTENTIATING THE ACTIVATION OF NK CELLS TRIALS IN COMBINATION IN VARIOUS SOLID AND HEMATOLOGICAL TUMORS UPCOMING DATA EXPECTED: END OF 2017

CO-DEVELOPMENT AND COMMERCIALIZATION AGREEMENT WITH ASTRAZENECA

ANTIBODY POTENTIATING THE ACTIVATION OF NK AND T CELLS

Monalizumab TRIALS IN MONOTHERAPY AND COMBINATION IN VARIOUS SOLID AND HEMATOLOGICAL **TUMORS** 

UPCOMING DATA EXPECTED: 2H 2017 / 1H 2018

PROPRIETARY PROGRAM

IPH4102

ANTIBODY AIMING TO SELECTIVELY DESTROY CANCER CELLS TRIAL IN CUTANEOUS T-CELL LYMPHOMA, AN ORPHAN DISEASE **UPCOMING DATA EXPECTED: 2Q 2017** 

A YEAR OF CLINICAL VALIDATIONS



## **CLINICAL PROGRAMS**

### **ENCOURAGING DATA FOR ALL DRUG CANDIDATES**



### **MONALIZUMAB**

#### IN PARTNERSHIP WITH ASTRAZENECA

Favorable initial safety data in monotherapy and in combination

EORTC-NCI-AACR<sup>1</sup> SYMPOSIUM - NOVEMBER 2016

Monotherapy - advanced gynecologic malignancies (18 evaluable patients) **AACR ANNUAL MEETING - APRIL 2017** 

Combination with cetuximab - recurrent /

metastatic squamous cell carcinoma of the head and neck (SCCHN) (17 evaluable patients) IN 2016. ASTRAZENECA INITIATED A TRIAL EVALUATING MONALIZUMAB IN COMBINATION WITH DURVALUMAB (ANTI-PD-L1) IN MORE THAN 200 PATIENTS WITH SOLID TUMORS.

Preclinical data presented at the AACR meeting in April 2016 confirmed the rationale for this trial by demonstrating that the combination of an anti-NKG2A with inhibitors of the PD-I/PD-LI pathway results in enhanced anti-tumor efficacy in preclinical models.

Further clinical trials are expected to be opened in the forthcoming months.

### **LIRILUMAB**

LICENSED TO BRISTOL-MYERS SQUIBB

**Encouraging interim efficacy data** SITC<sup>2</sup> ANNUAL MEETING - NOVEMBER 2016

Combination with nivolumab Cohort of patients with advanced SCCHN (29 evaluable patients) Objective response rate: 24%3 Complete response rate: 10%4

IN 2016, BRISTOL-MYERS SQUIBB PRESENTED THE FIRST CLINICAL DATA CONCERNING THE COMBINATION OF THE TWO THERAPEUTIC ANTIBODIES, ANTI-KIR AND ANTI-PD-1. THESE ENCOURAGING PRELIMINARY RESULTS LED TO AN EXPANSION, INCLUDING A RANDOMIZED COHORT, OF THE ONGOING TRIAL.

Data presented at the SITC meeting show preliminary signs of a potential clinical benefit of the combination of lirilumab with nivolumab in SCCHN, including complete responses in 10% of patients4. Within the frame of this non-randomized preliminary study, these findings suggest an increased antitumor response and improved survival, underlining the value of targeting both the PD-I and KIR pathways with nivolumab and lirilumab respectively. In this study, the safety profile of the combination of lirilumab with nivolumab is similar to that of nivolumab in monotherapy with the exception of an increased frequency of low grade infusion-related reactions. For the combination of lirilumab with ipilimumab, there did not appear to be additional safety concerns compared to ipilimumab monotherapy (data ESMO<sup>5</sup> 2016).

In February 2017, top-line results from the EffiKIR study<sup>6</sup> were disappointing (there was no statistically significant difference between either lirilumab arms and the placebo arm in terms of the primary endpoint, leukemia-free survival). However these findings do not call into question the program development potential, in particular in combination with other immune checkpoint inhibitors.

### EXPANSION OF THE TRIAL EVALUATING LIRILUMAB

### IN COMBINATION WITH NIVOLUMAB



### COULD YOU EXPLAIN WHAT THIS EXPANSION MEANS?

Early 2017, Bristol-Myers Squibb amended the clinical trial protocol of its Phase I/II trial evaluating lirilumab in combination with nivolumab in patients with advanced refractory solid tumors to include additional cohorts, among which a randomized cohort in squamous cell carcinoma of the head and neck (SCCHN) and the first triplet combination of immune checkpoint inhibitors: lirilumab - nivolumab - ipilimumab. The study could now recruit up to 650 patients (versus a previous maximum of 162) in Europe, the United States and Canada.

### SCCHN WOULD APPEAR TO BE THE PREFERRED INDICATION AT THIS STAGE?

The preliminary efficacy data presented in November in this indication were very encouraging. The next step is to demonstrate that lirilumab provides additional benefit in terms of efficacy compared to nivolumab alone through a randomized trial. The amended protocol plans on comparing the lirilumabnivolumab combination with nivolumab alone on an extended number of patients.

### WHAT IS THE IMPACT ON DEVELOPMENT?

In diseases with high unmet medical needs like cancer, the introduction of a randomized cohort in a Phase I study once signs of activity are obtained is a way of accelerating a clinical development process.

It is a major step forward in the trial evaluating lirilumab and we hope that the findings of this study, and more particularly of the randomized cohort in SCCHN, will confirm the expected clinical benefit for patients.

### **IPH4102**

### PROPRIETARY PROGRAM IN AN ORPHAN DISEASE

Preliminary safety and clinical activity data 3WCCL7 - OCTOBER 2016 AND ASH8 - DECEMBER 2016

Monotherapy - cutaneous T-cell lymphomas (CTCL) relapsed or refractory

Preliminary data from the dose escalation part of the study for the first 7 dose levels (16 evaluable patients)

Good safety profile - Global response rate: 38%, across all dosage levels ≤ 1.5 mg/kg

INITIATED LATE 2015, THE IPH4102 PROGRAM IS PROGRESSING QUICKLY. THE FIRST RESULTS PRESENTED IN 2016 ALLOW CONSIDERING THE BROADENING OF THE CLINICAL DEVELOPMENT PLAN AS EARLY AS 2018.

From the first 7 dose levels (out of 10), responses, including complete responses in skin and blood, were observed in some patients. These preliminary results provide hope for investigating physicians and patients (see page 14). The full results of the dose escalation part are expected in the second quarter of 2017. The dose escalation part will be followed by a cohort expansion.

7 Third World Congress of Cutaneous Lymphomas - 8 American Society of Hematology

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I European Organisation for Research and Treatment of Cancer - National Cancer Institute - American Association for Cancer Research - 2 Society for Immunotherapy of Cancer -

<sup>3 41%</sup> in patients with >1% PD-L1 expression - 4 Including confirmed and unconfirmed responses - 5 European Society for Medical Oncology - 6 randomized Phase II evaluating lirilumab as single agen maintenance treatment in elderly patients with acute myeloid leukemia.

## **CLINICAL PROGRAMS**

### **ENCOURAGING DATA FOR ALL DRUG CANDIDATES**



PROFESSOR MARTINE BAGOT,
PRINCIPAL INVESTIGATOR OF THE IPH4102
TRIAL AND HEAD OF DERMATOLOGY
DEPARTMENT AT THE SAINT-LOUIS
HOSPITAL, PARIS

## A RARE AND SERIOUS ILLNESS 6,000 NEW CASES IN EUROPE AND THE UNITED STATES PER YEAR

CTCL SUBTYPES	FREQUENCY	5-YEAR Survival rate
MYCOSIS FUNGOIDES (MF)	55 TO 65%	20 TO 95%
TRANSFORMED MF	~5%	≤15%
SÉZARY SYNDROME	~5%	~10%
CD30+ LYMPHOPROLIFERATIVE DISORDERS	15 TO 20%	76 TO 96%
OTHER	≤10%	≤20%

Sézary syndrome and transformed mycosis fungoides are the most aggressive CTCL subtypes

### **IPH4102: NEW HOPE FOR PATIENTS**

## COULD YOU EXPLAIN THE CHALLENGES OF TREATMENT FOR CUTANEOUS T-CELL LYMPHOMAS?

Currently, there is no curative treatment in the advanced stages of the disease (see box below). The treatments available only provide partial or transient remissions. We can administer up to four successive lines of treatment; beyond that, we are powerless. There is a real need for new therapeutic options. Several innovative drug candidates, all monoclonal antibodies, are currently in development, with two approaches: those that destroy tumors and those that stimulate the patient's immune system. IPH4102 is in the first category.

#### **HOW DOES IPH4102 GIVE CAUSE FOR HOPE?**

First, because its target is expressed in a really specific way and on the majority of tumor cells. In theory, this should allow for a good level of efficacy paired with good safety. This seems indeed to be the case in the study we are conducting: we do not observe immunosuppression in patients, unlike other approaches.

As the drug candidate had never been administered to humans, we started at very low doses to study its safety. The results we have obtained so far are very good, without any treatment-related severe adverse events. In this early phase, we have observed very encouraging efficacy in skin and blood. Until now, data are interesting, in particular in light of the fact that the trial included patients in the advanced stages of the disease, primarily patients with Sézary syndrome, and that these patients had received all available treatment options.

#### HOW DO YOU SEE THE NEXT PHASE OF THIS PROGRAM?

The full results of the dose escalation will be available during the second quarter of 2017. In the meantime, we are preparing the cohort expansion part that plans to treat 30 patients, split equally between patients with Sézary syndrome or transformed mycosis fungoides. In parallel, we accompany Innate Pharma in its reflection on the drug development strategy. It is a major challenge for patients and we want to do all we can so that they can have faster access to treatment.

# STRENGTHENED RESOURCES

THE ENCOURAGING RESULTS OBTAINED IN THE DIFFERENT PROGRAMS IN 2016 WILL GENERATE NEW STUDIES, IN MONOTHERAPY OR IN COMBINATION, AND MORE ADVANCED TRIALS INVOLVING AN INCREASING NUMBER OF PATIENTS. THE CLINICAL TEAM HAS BEEN REINFORCED TO ENSURE THE SUCCESS OF THIS BUILDUP IN OPERATIONS.

The clinical team combines complementary skills to ensure the end-to-end monitoring of trials:

- Physicians design the trials in conjunction with hospital practitioners, taking into account the strategic objectives of the programs. They also play a central role for the interpretation and reporting of the results;
- Regulatory affairs organize interactions with health agencies before, during and after the trial, up to registration steps and beyond;
- Pharmacovigilance continuously monitors the safety and tolerability data coming from investigating centers;
- Clinical operations ensure the smooth running of the trials (exchanges with investigator centers, treatment supply, collection of data and samples...) in constant contact with the specialized CROs<sup>9</sup> and the referring physician.
- 9 Contract Research Organization, specialized in research and clinical development

## A TEAM DEDICATED

## TO TRANSLATIONAL RESEARCH



MATHIEU BLÉRY, R&D SENIOR DIRECTOR, TRANSLATIONAL RESEARCH

#### WHAT IS THE PURPOSE OF TRANSLATIONAL RESEARCH?

Translational research is a strategic axis of immuno-oncology R&D. From samples of patients' tissues, our goal is to identify relevant biomarkers to determine patient profiles responding to certain types of treatment in each indication with the aim of setting up personalized immunotherapy strategies, ie matching the optimal treatment for each type of patient. With the development of combination therapies, this type of knowledge becomes even more important.

Concretely, our main missions are:

- to validate research hypotheses according to target groups, pathologies and patient categories;
- to identify biomarkers that could be used to select the patients who would best respond to certain treatments;
- to carry out tests required for authorization to initiate clinical studies or drug registration;
- to follow-up biological parameters of patients receiving treatment with our drug candidates.

### WHY DID YOU CREATE A DEDICATED TEAM NOW?

We have always conducted translational research within our different programs. With the advancement and expansion of our drug portfolio, dedicate an identified team allows us to have a more global approach and more specific competences. We are also strengthening and structuring our relations with the medical centers that treat patients and collect samples.

### YOU HAVE STARTED A PARTNERSHIP WITH THE AP-HM (MARSEILLE PUBLIC HOSPITALS) IN 2016, WHAT IS THE OBJECTIVE?

The AP-HM is a recognized player in immuno-oncology clinical research. By strengthening our exchanges with the clinicians, our goal is to better understand patients' responses to different treatments in order to bring them new therapeutic options that exceed the limits of current treatments.

This is why we are working closely with many expert centers, in France and worldwide, such as the Saint-Louis Hospital (Paris) or the Léon Bérard center (Lyon).

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"WE CONTINUE TO BUILD ON OUR UNIQUE AND INNOVATIVE SCIENCE TO EXPAND OUR PORTFOLIO WITH NEW DRUG CANDIDATES IN ORDER TO ADDRESS UNMET MEDICAL NEEDS IN CANCER."

NICOLAI WAGTMANN EXECUTIVE VICE PRESIDENT, CHIEF SCIENTIFIC OFFICER

# A YEAR TO BUILD THE PORTFOLIO OF PRECLINICAL PROGRAMS

# 3 PRECLINICAL PROGRAMS IN ONCOLOGY

IPH4301 ANTI-MICA/B DUAL MECHANISM OF ACTION: STIMULATE THE IMMUNE RESPONSE AND ACT DIRECTLY ON THE DESTRUCTION OF TUMOR CELLS IND-ENABLING STUDIES

IPH52

ANTI-CD39

IPH53

**ANTI-CD73** 

RESTORE A PRO-INFLAMMATORY TUMOR MICROENVIRONMENT TO STIMULATE THE IMMUNE RESPONSE RESEARCH



## MONOCLONAL

- DESTROY TUMOR CELLS OR ACTIVATE IMMUNE CELLS
- BY CONNECTING WITH SPECIFIC
   RECEPTORS OF THE TARGETED CELLS



## ANTIBODY DRUG

- BRING A DRUG INSIDE A TUMOR CELL TO DESTROY IT
- BY LINKING IT WITH AN ANTIBODY THAT SPECIFICALLY RECOGNIZES THE TUMOR





- DESTROY TUMOR CELLS
- BY BINDING BOTH WITH A TUMOR ANTIGEN AND WITH AN NK CELL RECEPTOR

## PRECLINICAL PROGRAMS

### AN EXPANDED PORTFOLIO

**TARGET** 



RESEARCH



IND-ENABLING STUDIES



**CLINIC** 

### TWO NEW PROGRAMS IN TUMOR MICROENVIRONMENT

In 2016, Innate Pharma initiated two new preclinical programs: IPH52 (first-in-class anti-CD39, acquired from Orega Biotech) and IPH53 (anti-CD73<sup>10</sup>, in the frame of the TumAdoR European project). Both target the tumor microenvironment and the ATP/adenosine pathway. With this approach, the Company is expanding its market position and exploring complementary mechanisms of action potentially synergetic with the targeting of NK and T cells or with other therapeutic agents.

### PROGRESS OF IPH4301 PROGRAM

The first-in-class IPH4301 (anti MICA/B) program is currently undergoing IND-enabling studies, and could enter the clinic in 2018. As a result of the frequent expression of MICA/B by tumor cells in many therapeutic indications such as breast, lung, prostate or colorectal cancer, this program has a broad clinical potential.

### DEVELOPMENT OF NEW ANTIBODY FORMATS

Thanks to its technology platforms, Innate Pharma is developing new antibody formats that could contribute to expanding the Company's proprietary programs portfolio such as bispecific antibodies engaging NK cells<sup>11</sup>.

These bispecific formats can be subject of non-exclusive license agreements. This is the case of the partnership with Sanofi, established in January 2016.

## FUTURE AVENUES FOR IMMUNOTHERAPY TREATMENTS FOR CANCER

### THERAPEUTIC COMBINATIONS OFFER NUMEROUS OPPORTUNITIES

Today anti-PD-I/PD-LI checkpoint inhibitors are becoming the standard of care in several cancer indications. However, only a minority of patients respond to these treatments, which leads to exploring new immunotherapy strategies that may help a greater number of people. Many trials are ongoing, notably testing combinations between antibodies targeting immune checkpoint inhibitors on different cell types, as well as combinations between immunotherapy and cytotoxic antibodies or chemotherapies or other targeted therapies.

This combination approach offers multiple opportunities for Innate Pharma's molecules that specifically target the cells and mechanisms of the innate immune system, primarily NK cells. Yet, NK cells are not only able to destroy tumor cells but also to activate other immune cells, including T lymphocytes, which are the direct target of

the anti-PD-I/PD-LI checkpoint inhibitors. The partnerships signed with Bristol-Myers Squibb and AstraZeneca are based on this rationale for combining checkpoint antibodies targeting NK cells with those targeting T cells, and several trials are currently ongoing in combination with other therapeutic agents. This combinatorial approach should be extended even more in the future.

### TAKE ACTION AT SEVERAL LEVELS OF THE IMMUNE RESPONSE CHAIN

The two programs IPH52 and IPH53 could also play a part in this combinatorial approach. Both programs target complementary receptors that block the mechanisms that inhibit the immune response in the environment surrounding tumors. Preclinical data suggest that they could also be combined with other treatments, such as PD-1 blockers or chemotherapies.

This program is developed within the TurnAdoR project (www.turnadoreu) coordinated by Dr C. Caux (Léon Bérard Center and Center of Research in Cancerology Lyon), and funded under the European Community's seventh framework program under agreement n°602200. - II

## A STRUCTURED APPROACH

## TO EXPANDING THE PORTFOLIO



YANNIS MOREL, EXECUTIVEVICE PRESIDENT, CHIEF BUSINESS OFFICER

## WHAT ROLE DOES THE ACQUISITION OF NEW TARGETS AND PROGRAMS PLAY IN YOUR STRATEGY TO EXPAND THE PORTFOLIO?

Our commitment to enhance our portfolio is strong and the identification of targets and drug candidates is an important contribution to this enlargement strategy. Our approach is structured and we want to be proactive in increasing the number of partnerships.

## IN WHAT WAY IS THE PARTNERSHIP WITH OREGA BIOTECH, SIGNED IN 2016, REPRESENTATIVE OF THIS STRATEGY?

It embodies our change in status, of course, since we are now an industrial partner for biotechs in earlier stages of development, where we were ourselves a few years ago. Above all, it marks a strategic shift, as it is our first acquisition of an external program. We had already acquired licenses on technologies or targets, that were used in the development of our candidates internally. Here, though there is still much to be done, we have acquired an entire project.

### WHAT ARE YOUR RELATIONS WITH ACADEMIC RESEARCH?

Innate Pharma comes from academic research and we have always had strong links with many teams working in our areas of expertise. As we develop our business, not only are we are strengthening our internal research capabilities, we are also increasing our partnerships with academic laboratories, which broadens the opportunities available.

### AT WHAT STAGE OF A PROJECT DOES THE BUSINESS DEVELOPMENT TEAM TAKE ACTION?

We are convinced that collaborative partnerships are a source of value creation for everyone. Innate Pharma is active at every stage of a project. Our teams have acquired the experience and expertise that allow us today to establish partnerships for both the license of some of our programs to pharmaceutical companies and for the acquisition of targets and projects, whether they are academic or industrial.

## 2016,

### A YEAR TO SHOWCASE INNATE PHARMA'S RESEARCH

In line with the progress of its programs, Innate Pharma and its partners presented preclinical and clinical results at major scientific and medical congresses all along the year.

AACR APRIL 2016	ASCO JUNE 2016	ESMO 0CT 2016	3WCCL OCT 2016	SITC NOV 2016	EORTC-NCI-AACR NOV 2016	ASH DEC 2016
MONALIZUMAB		LIRILUMAB		LIRILUMAB		LIRILUMAB
IPH4301	IPH4102		IPH4102	MONALIZUMAB	MONALIZUMAB	IPH4102
IPH52 / IPH53						

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"INNATE PHARMA IS INCREASINGLY RECOGNIZED IN ITS FIELD AND WE ARE ABLE TO ATTRACT HIGH-LEVEL AND INTERNATIONAL PROFILES"

NATHALIE DEVESA IVARS, HUMAN RESOURCES DIRECTOR

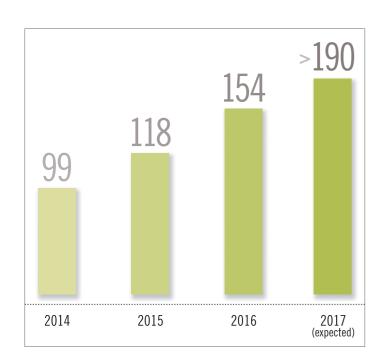
# 2016

## A YEAR OF GROWTH AND INTEGRATION



## **MANAGEMENT & ORGANIZATION**

### RECRUITING AND INTEGRATING TALENTS



HEADCOUNT EVOLUTION

### The growth in staff continues at a rapid pace

After about twenty recruitments in 2015, the pace accelerated in 2016 with nearly 40 new employees. The Company's headcount increased by more than 80% in 4 years and by more than 50% in 2 years. These recruitments correspond to:

- The strengthening of research and development activities, in relation to the development of new preclinical programs such as IPH52 and IPH53, or the progress of IPH4301;
- The increase in clinical development activities, with the arrival of several physicians in charge of the design and supervision of different trials, as well as the strengthening of the regulatory affairs, pharmacovigilance and operational management teams;
- The strengthening of management for all Company's activities.



The Company's attractiveness progresses nationally and internationally

Recruiting suitable profiles is a challenge for Innate Pharma, in a sector where experts profiles - in immunology, CMC (chemistry, manufacturing and controls), preclinical development, clinical operations or regulatory affairs, to name but a few - are rare.

To strengthen its internal skills, Innate Pharma benefits however from a growing reputation and attractiveness. The Company is increasingly identified as a key player in the field of cancer immunotherapy. Its scientific and entrepreneurial project is becoming more attractive as the Company's growth path offers medium-term career prospects. Furthermore, Innate Pharma benefits from the broader image of Marseille Immunopole that is gaining international recognition.



Rapid integration of new skills: a challenge met thanks to the commitment of all the teams

The rapid growth in headcount brings about a recomposition of teams and an increased need for middle management. Fully committed to the success of the Company project, Innate Pharma's employees have made a strong contribution to the successful integration of new recruits.

The teams have demonstrated flexibility and investment in these developments. A work is carrying out to redefine jobs and several employees progressed to management positions, benefitting from appropriate training and mentoring. The Company also made sure to mix junior and more experienced profiles and paid specific attention to the conditions of installation of new staff from outside the region, a key factor of successful integration.



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## DEVELOPING THE ORGANIZATION AND CULTURE OF THE COMPANY



### Adapting the organization to growth

Innate Pharma has been built on a strong collaborative culture, with the desire to engage all the internal stakeholders in the company project. With the growth in headcount, the challenge is to maintain the commitment without weighing down the process.

The Company has undertaken substantive work to adjust its organization: some teams have been split in order to maintain flexibility and coherence at each level, to allow the follow-up and sharing of information as closely as possible to the teams. This development is accompanied by actions fostering cohesion, at the level of each team and on a cross-functional basis within the Company.

### Innate Pharma invests for quality of work life

Located in the heart of the Calanques National Park, Innate Pharma's headquarters are surrounded by a privileged environment.

To accommodate the growth, Innate Pharma has undertaken a project for the construction of a new building next to the existing one to welcome all staff. It will be mainly dedicated to offices and common spaces whereas the current building will be entirely dedicated to research laboratories.



### PREPARING TOMORROW'S TALENTS

Teaching and training, a pool of expertise for Innate Pharma

In conjunction with the territory's educational establishments, Innate Pharma is involved in the training of students which provides a real talent pool.

The Company regularly welcomes groups of students for visits and vocational presentations or in the framework of internships and work-study contracts. The Company also contributes to structuring the training offer in immunology. This close relationship with students and schools facilitates the integration of young graduates in the professional world and, for companies, the recruitment of rapidly operational skilled candidates.





### MAXIME DEVITA, ITTECHNICIAN AND WORKS COUNCIL SECRETARY

### **OPENING THE COMPANY'S DOORS**

### TO STUDENTS FROM HIGH-PRIORITY AREAS

## WHY DID YOU GET INVOLVED IN THIS PROJECT?

I joined Innate Pharma after obtaining a vocational degree. A native of Marseille, I had never heard of this company, or even research centers or cuttingedge scientific companies. I

discovered a professional and exciting environment that offers opportunities at very different levels of qualification. During my personal history, I have met young people, from priority areas, who neither receive support from their family nor have the resources needed to enter the business world with confidence. I am committed to showing them that opportunities exist and that it is worth investing oneself in school.

### WHAT DOES THE ACTION INITIATED ENTAIL?

By giving these students the opportunity to gain insight into both the world of business and research at Innate Pharma, we want on the one hand to motivate them to pursue their studies up to the high school diploma and higher education and, on the other hand, to show them that everyone can find his place inside the company.

#### **CONCRETELY, HOW IS THIS ORGANIZED?**

Our aim is to build a lasting relationship between students and Innate Pharma's employees: Company visits are organized, with a presentation of all jobs, scientific or not, and we welcome ninth grade student for internships. From September 2017, we will start a class mentoring program by employees.

### WHAT ARE THE FIRST RESULTS?

The stakeholders involved, whether the students, their teachers or Innate Pharma's employees, are enthusiastic and other companies in the Luminy area have joined this initiative. Teachers told us that students have really impressed the board of examiners thanks to the quality of their presentations. There is a real commitment by the Management and Human Resources department in this desire to inspire young people and to open new perspectives for them. It is the first year, but we fully intend to continue and expand our commitment.

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"OUR SOLID CASH POSITION GIVES US THE MEANS TO PURSUE OUR DEVELOPMENTS AND TO INVEST IN OUR AMBITIOUS PROJECTS."

LAURE-HÉLÈNE MERCIER, EXECUTIVE VICE PRESIDENT, CHIEF FINANCIAL OFFICER A YEAR OF ROBUST FINANCIAL POSITION FOR FURTHER GROWTH

## **GOVERNANCE**

DUAL GOVERNANCE AND THE DIVERSITY OF THE SUPERVISORY BOARD MEMBERS ENSURE THAT THE INTERESTS OF ALL THE STAKEHOLDERS ARE TAKEN INTO ACCOUNT.

### **SUPERVISORY BOARD**

Members are elected for a two year period and all current mandates expire in 2017. The composition presented below, including the nomination of two new members, is submitted for approval at the Annual General Meeting on June 23, 2017.



HERVÉ BRAILLY, CHAIRMAN CO-FOUNDER AND FORMER CHAIRMAN OF THE EXECUTIVE BOARD, INNATE PHARMA



IRINA STAATZ-GRANZER, **VICE CHAIRMAN** FOUNDER AND CEO, STAATZ BUSINESS **DEVELOPMENT & STRATEGY** 



**GILLES BRISSON** FORMER CHAIRMAN OF THE EXECUTIVE BOARD AND FORMER CHAIRMAN OF SUPERVISORY BOARD, AVENTIS PHARMA SA



**VÉRONIQUE CHABERNAUD** FOUNDER AND CEO, "CRÉER LA VITALITÉ"



**MAÏLYS FERRERE, REPRESENTING BPIFRANCE PARTICIPATIONS** DIRECTOR OF LARGEVENTURE INVESTMENT ACTIVITY OF BPIFRANCE



KARSTEN MUNK KNUDSEN, REPRESENTING NOVO NORDISK A/S SENIOR VICE PRESIDENT CORPORATE FINANCE, NOVO NORDISK A/S



**PATRICK LANGLOIS** GENERAL PARTNER, PJL CONSEILS



**IEAN-CHARLES SORIA** HEAD OF DRUG DEVELOPMENT DEPARTMENT AT GUSTAVE ROUSSY CANCER CENTER



**OLIVIER MARTINEZ, OBSERVER** (NON-VOTING MEMBER) SENIOR INVESTMENTS DIRECTOR, INVESTMENTS BIOTECH DEPARTMENT. DIRECTION OF INNOVATION, BPIFRANCE



### HERVÉ BRAILLY, YOU HAVE TAKEN THE CHAIRMANSHIP OF THE SUPERVISORY BOARD. WHAT WILL BE YOUR NEW ROLE?

The Executive Board determines and implements the strategy and ensures the conduct of business, whereas the Supervisory Board validates the strategic choices, controls the management and takes into consideration the interest of all stakeholders. I personally am attached to this dual governance system. As Chairman, I guide the Supervisory Board's work and conduct the debates. Collectively, we contribute our expertise to the Executive Board to drive the Company's strategy.

### WHAT ARE THE CHANGES WITHIN THE SUPERVISORY BOARD?

As of their appointment by the Annual General Meeting on June 23, 2017, we will welcome two new members. First Bpifrance, represented by Maïlys Ferrere. We are pleased that Bpifrance, one of our long-standing shareholders, that has supported us for many years, is now a full member of the Board. Next, Professor Jean-Charles Soria, one of the leading French cancer specialists, who is the voice of both carers and patients. The diversity of profiles within the Board is a source of wealth and an asset, as, beyond the representativeness of all our stakeholders, the expertise and experience of each of its members contribute to fuelling the Board's work.

### **BOARD COMMITTEES**

THE ASSIGNATION TO ONE OR SEVERAL COMMITTEES WILL BE DECIDED BY THE SUPERVISORY BOARD FOLLOWING THE ANNUAL GENERAL MEETING. THE FOLLOWING COMMITTEES ARE EFFECTIVE UNTIL JUNE 23, 2017:

	AUDIT COMMITTEE	REMUNERATION & APPOINTMENTS COMMITTEE	TRANSACTIONS Committee
Hervé BRAILLY, Chairman	•	•	
Irina STAATZ-GRANZER, Vice President	•		*
Gilles BRISSON	•	*	•
Véronique CHABERNAUD		•	
Mailys FERRERE, representing Bpifrance Participations			
Karsten Munk KNUDSEN representing Novo NORDISK A/S			•
Patrick LANGLOIS	*	•	
Jean-Charles SORIA			
Olivier MARTINEZ, observer (non-voting member)			

<sup>\*</sup> Chairman 

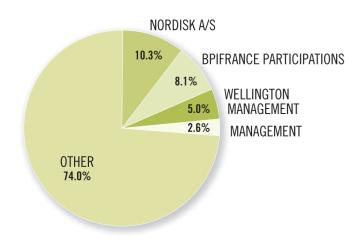
Member

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## **SHAREHOLDERS**

### SHAREHOLDING STRUCTURE

AS OF MAY 5, 2017



# Innate Pharma has always cared about associating its employees with the Company's operational and stock performances. In 2016, this policy was strengthened thanks to discussions held between the Management, the Remuneration Committee and the

A MEANS TO COLLECTIVE PERFORMANCE

EMPLOYEE SHAREHOLDING.

union representatives.

Employee shareholding aims at attracting, retaining and motivating employees through the distribution of equity instruments that give the right, subject to the employee's presence, to ordinary shares.

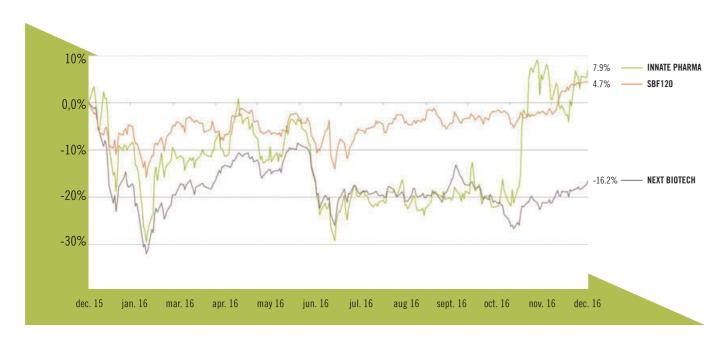
Since 2016, there have been two kinds of equity nstruments:

- the distribution of free shares, to reward the achievement of the annual collective objectives, based on the operational performance criteria, and;
- the distribution of free preferred shares, to reward long-term performance. Long-term performance is assessed according to the evolution of stock price over a period of 3 years, which is closely linked to the Company's operational results, and allows employees' collective interests to be aligned with those of shareholders.

### **STOCK MARKET**

In 2016, the Innate Pharma share experienced several fluctuations. The share first followed the drop in the biotech sector, before picking up sharply following different presentations of clinical results in the Fall. In December, the announcement of changes in the governance and management was well received by the market. The

biotech sector as a whole had a more difficult year, the European index Next Biotech slipped by -16% and the Nasdaq Biotech Index (NBI) by -21%. At the same time, the SBF 120 index progressed by 4.7%. In total, the Innate Pharma share progressed by 7.9% in 2016. In 5 years, the share price increased more than tenfold.





## FINANCIAL ELEMENTS

## THE 2016 RESULTS INDICATE THE MATURATION OF THE COMPANY AND ITS CAPACITY TO FINANCE ITS MEDIUM-TERM DEVELOPMENT STRATEGY

The Company's development is reflected in the progression of revenue and other income which reach €65.7m, versus €25.1m in 2015. They include €41.6m related to the monalizumab program. This element doesn't impact the cash position: it corresponds to the spreading of the initial payment of \$250m received in June 2015. It is recognized as the program progresses in the framework of the codevelopment and commercialization agreement with AstraZeneca/MedImmune. The revenue and other income also include a payment of \$15m (€13.8m) from Bristol-Myers Squibb for the lirilumab program, in line with the results presented in November 2016 at the SITC meeting.

The progress of preclinical programs and especially clinical programs can also be seen in the strong increase

in operating expenses that reach €58.2m (of which 84% for R&D expenditures). The expenditures cover both subcontracting costs, mainly linked to clinical trials, and the staff growth. It should be recalled that the headcount increased by 30% over the period.

As a consequence, Innate Pharma recorded in 2016 a positive net result, with a profit of €12.6m.

With a cash position of €230.7m as of December 31,2016, not including the milestone payment of \$15m from Bristol-Myers Squibb effectively received in January 2017, Innate Pharma has sufficient resources to finance its ambitious development plan for the coming years.

## SELECTED FINANCIAL NUMBERS

(IN THOUSAND EUROS, IFRS)

YEAR ENDED 31 DECEMBER	2016	2015
Revenues from collaboration and licensing agreements	56,159	17,906
Government financing for research expenditures	9,561	7,235
Revenue and other income	65,721	25,141
Research and Development expenses	(48,628)	(29,906)
General and Administrative expenses	(9,522)	(6,008)
Operating expenses	(58,150)	(35,914)
Operating income / (loss)	7,571	(10,772)
Financial income / (expenses), net	5,370	4,066
Income tax	(301)	-
Net income / (loss)	12,640	(6,706)
Cash, cash equivalents and financial assets	230,664	273,704
Total financial debt	5,327	3,754

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### **CONTACTS**

business@innate-pharma.com corporate@innate-pharma.cominvestors@innate-pharma.comjobs@innate-pharma.com medical@innate-pharma.com press@innate-pharma.com science@innate-pharma.com



117 avenue de Luminy - Marseille, 13276 - FRANCE Tel. +33 (0)4 30 30 30 30 - Fax +33 (0)4 30 30 30 00 info@innate-pharma.com