Spotlight on Investor Relations

Innate Pharma launched its shareholders' club 'Innate en Actions' in April 2012

Since its IPO on Euronext Paris (2006), Innate Pharma has endeavored to provide its shareholders with accurate, detailed information in compliance with the best practices of financial communications.

Supported by its individual shareholders, Innate Pharma intends to pursue consolidating relations with its shareholders, which was the idea behind the creation of 'Innate en Actions', Open to private individuals only, the club proved to be a great success with more than a hundred applicants registered in them were warmly welcomed by Innate Pharma at a meeting held on site in September. A visit of the offices and laboratories was organized, together with a meeting with the CEO, Hervé Brailly, with the manager in charge of the IPH21 and IPH41 programmes, and the Investor Relations team.

You can join the 'Innate en Actions' club here:

pharma.com/fr/finances/clubactionnaires

(in French only)

Crossing of threshold (Sept. 5, 2012)

OGBBA Van Herk BV, a company incorporated under Dutch laws, reported to the French Authority (AMF) that it crossed over the 5% threshold of the share capital and voting rights of the Company. The crossing of this threshold results from the purchase of IPH shares on the market. OGBBA Van Herk BV announced that it held 2 335 380 shares representing 6.16 % of the capital and voting rights of Innate Pharma

OCTIPPOCIO & DES PRODUITS FINANCIERS

November 23 & 24, 2012 > 15th Actionaria forum

Innate Pharma will be present for the second time at Actionaria, a forum dedicated to individual shareholders.

Where to meet us next?

Innate Pharma's IR team will be on the East Coast of the United States in the first week of December and on the West Coast in the second week of January. The Company will also be present at the Oddo Midcap Forum in Lyon on January 11.

Shareholders and board representation



NEWSLETTER TO **SHAREHOLDERS**

Product News:

IPH2102/BMS-986015:

- First Phase I combination trial in various solid tumors
- First Phase II, single agent trial in Acute Myeloid Leukemia

'Innate en Actions'

The Innate Pharma shareholders' club launched in April 2012

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EDITORIAL

Dear Shareholders.

I am happy to be back again during this very busy month of November. As you will discover herein, a number of important events for Innate have already taken place this year. First and foremost, a little more than a year after signing our first partnership with Bristol-Myers Squibb, the anti-KIR programme has successfully completed several key stages, with a Phase II trial soon to begin in Acute Myeloid Leukemia, together with a Phase I trial in combination in a variety of solid tumors.

The immuno-oncology sector continues to draw attention. It was in the limelight at the American Society of Clinical Oncology (ASCO) international meeting in June. It also very recently garnered recognition by the prestigious Prix Galien USA, honoring the best biotech product, which was awarded to the anti-CTLA-4 monoclonal antibody, YERVOY® (ipilimumab), of Bristol-Myers Squibb.

Investors Relations Laure-Hélène Mercier,

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€ 3.0

€ 2.1

€ 3.0

€ 2.4

€ 3.5

innate pharma



November 2012

- Editorial
- The Innate Pharma scene in 2012
- R&D and Science News
- 12: Innate Science: mAb targeting innate immunity
- Investor News

We celebrated the 2011 Nobel Prize in Medicine awarded to researchers for their work on innate immunity by organizing a dedicated roundtable with Bristol-Myers Squibb in Paris in May. This event proved to be extremely productive in terms of the discussions and opinions on how immunotherapy can contribute to treating cancer over the next decade.

On a completely different level, we have been particularly active on investor relations over the past 12 months, whether with institutional investors whom we have met several times in France, Europe and the US, or with individual investors for whom we set up a shareholders' club last spring.

Innate's overperformance on the stock market over the past two years can only encourage us to keep going!

Thank you for your confidence!

23 24 NOVEMBRE 2012 Palais des Congrès de Paris

HERVÉ BRAILLY. Chairman of the Executive Board **Chief Executive Officer**

Innate's Products Pipeline (3Q 2012)

PROGRAM	TARGET	INDICATION	STATUS	PARTNER	NEXT MILESTONE
IPH2102/ BMS-986015	KIR2DL1,2,3	Acute Myeloid Leukemia	Phase II	Bristol-Myers Squibb	First patient inclusion
		Solid tumors, combination with anti-PD-1	Phase I	Bristol-Myers Squibb	Phase I completion
IPH2201/ NN8765	NKG2A	Rheumatoid arthritis	Phase I	Novo Nordisk A/S	Entry in Phase II
IPH41	KIR3DL2	Cutaneous T-cell Iymphoma	Preclinical research	In house	Lead candidate selection
IPH33	TLR3	Inflammation, autoimmunity	Preclinical research	In house	Lead candidate selection
Discovery 1	Undisclosed	Cancer / Inflammation	Target validation	In house	
Discovery 2	Undisclosed	Cancer	Target validation	In house	One new program with target validation
Discovery 3	Undisclosed	Cancer	Target validation	In house	and candidate per year
Discovery 4	NKp46	Cancer / Inflammation	Target validation	In house	

Innate Pharma's programmes newsflow

IPH21, licenced to Bristol Myers-Squibb in July 2011 and the most advanced of our programs, is in the spotlight.

First Phase I combination trial in various solid tumors See press release (October 30, 2012)

This trial will test IPH2102/BMS-986015 in a variety of solid tumors and in combination with the anti-PD-1 antibody BMS-936558.

The purpose of this Phase I open label study is to determine whether the combination of IPH2102/BMS-986015 and BMS-936558 is safe and provide preliminary information on the clinical activity of the combination.

It will be conducted in two parts - dose escalation and cohort expansion - and is expected to enroll approximately 150 patients. During cohort expansion, tumor type will be restricted to the following advanced malignancies: Non-Small Cell Lung Cancer - squamous and non-squamous histology, Renal Cell Carcinoma, Melanoma, Colorectal Cancer and Serous Ovarian Carcinoma.

Marcel Rozencweig, Chief Medical Officer of Innate Pharma, said: "IPH2102/BMS-986015 will be tested in a variety of solid tumors, in combination with anti-PD-1 which has shown promising single agent results in Phase I/II trials."

Results of the Phase I trial of IPH2101* (hybridoma anti-KIR antibody) in elderly patients with Acute Myeloid Leukemia in first complete remission published online in the journal Blood See press release (October 18, 2012)

The trial featured a dose-escalation protocol with seven dose levels (from 0.0003 to 3 mg/kg with 3 patients per dose level) and a single dose administration. The objective was to determine a safe and pharmacologically active dose. Twenty three patients were enrolled in this study. Good tolerance was observed at all tested doses of IPH2101, adverse events were mild and transient. The maximum tolerated dose was not reached.

Median progression free survival, relapse free survival and overall survival were respectively: 7.7 months, 10.8 months and 12.7 months. The 6 patients treated at dose levels I and 3 mg/kg showed a significantly improved overall survival compared to the 16 patients of the previous dose levels (<0.3 mg/kg).

Dr. Norbert Vey, MD (Institut Paoli Calmettes, Marseille), lead investigator of the Phase I trial in AML, said: "With this trial, we have shown that full KIR occupancy is reached and maintained for time periods (day to several weeks) that depend on the dose and without reaching the maximum tolerated dose. Results from the study support continuing investigation of anti-KIR mAbs in AML''.

* See section "About IPH2102/BMS-986015 and IPH2101" in the press release

New target NKp46

In January, the Company announced the discovery of a novel immune regulation mechanism involving the NKp46 receptor on Natural Killer cells. It was described and published in Science magazine by team from the CIML, a key academic partner of Innate Pharma. Innate Pharma co-owns intellectual property rights relating to this discovery with INSERM, the French National Institute of Health and Medical Research.

See press release (Janualry 20, 2012)

See the interview of Eric Vivier and Sophie Ugolini on http://vimeo.com/35305550



First Phase II, single agent trial in Acute Myeloid Leukemia See press release (September 4, 2012)

Innate Pharma received regulatory authorization to start a double-blind placebo-controlled randomized Phase II trial of IPH2102/BMS-986015 as maintenance treatment in elderly patients with Acute Myeloid Leukemia in first complete remission (study IPH2102-201, the "EffiKIR" trial).

The protocol calls for inclusion of 150 patients, randomized into three arms. Two arms will test single agent IPH2102/BMS-986015 at different doses and one arm will receive placebo. The primary efficacy endpoint is leukemia-free survival. Secondary endpoints include safety and overall survival.

This trial is sponsored by Innate Pharma and will be performed in France, with the participation of the two French clinical cooperative groups, ALFA and GOELAMS*, harnessing the research effort of the French centers qualified to treat patients with AML. The principal investigator is Dr. Norbert Vey.

First patient inclusion is expected before the end of the year.

* ALFA : Acute Leukemia French Association. GOELAMS : Groupe Ouest-Est des Leucémies Aiguës et Maladies du Sang (Acute Leukemia and Blood Diseases West-Est Group)



EffiKIR positionning

Over the past 12 months, the Company's expertise in innate immunity has been in the spotlight thanks to the 2011 Nobel Prize in Medicine which was awarded to three researchers having contributed to its discovery.

In January, one of Innate Pharma's co-founders and Director of the Marseille-Luminy Immunology Centre (CIML), Eric Vivier, also published an article in the journal Science on a new mechanism that controls NK cells and involving NKp46 (see above).

These progresses in the field of innate immunity improve the Company's visibility, as well as strengthen its position as a leading industry player in that field.

On October 17, Yervoy®, a monoclonal antibody developed by Bristol-Myers Squibb, received the prestigious prix Galien USA award for the best biotech product of 2012. Yervoy® was the first drug to gain approval for metastatic melanoma in the last 10 years.

This prize was awarded by a first-class scientific committee including several Nobel Prize winners. It recognizes the technical, scientific and medical capacities required to develop innovative drugs. The Prix Galien is considered to be the most prestigious prize in biopharmaceutical research and development.

In May, Bristol-Myers Squibb and Innate Pharma co-organized an international roundtable on innate immunity.

Innate Pharma co-organized a special roundtable with Bristol-Myers Squib France this May at the Paris Oceanographic Institute: "Innate immunity - From Revolutionary Discovery to Therapeutic Revolution". With Bruce Beutler and Jules Hoffman - the 2011 Nobel Prize winners in Medicine - as its guests of honor, this event clearly stressed the importance of immunology and innate immunity in treating cancer patients.

The roundtable was a roaring success thanks to its 150 international participants from the scientific and medical communities.

Source: news.bms.com





You can watch a video of the event and download the summary of the roundtable at: http://www.immunite-innee.com/fr/

Immunotherapy makes the headlines again at the ASCO Annual Meeting in June 2012

This year again, immunotherapy was a headliner at the ASCO annual meeting and especially "antigen-independent immunotherapy". This concerns a series of new approaches using antibodies that activate immune cells so they work against the cancer. The principle: the immune system has inhibitory mechanisms that prevent its over-activation which are exploited by the tumor to help it grow. These negative checkpoints of the immune response therefore need to be blocked. This is the main idea behind the development of anti-KIR by Innate Pharma, and which has demonstrated its efficacy with Yervoy® (BMS) and presented some very interesting early results at the last ASCO annual meeting with the anti-PD-I of Bristol-Myers Squibb.

I²: INNATE SCIENCE: mAb targeting innate immunity

For our 10th shareholder newsletter, we have chosen to describe the technical approach behind the programmes developed by Innate Pharma: fully human or humanized monoclonal antibodies (mAb).

Manipulating the immune system's checkpoints by means of antibodies is a very innovative approach since it was only recently validated in 2010 by the clinical results of the first authorized drug using this mechanism of action: ipilimumab (Yervoy®, Bristol-Myers Squibb). This product targets the CTLA-4 receptor found in T-cells – killers of the adaptive immune system. In 2011, it became the first drug to be approved for metastatic melanoma (skin cancer) in the last decade.

Manipulation of the immune system's control pathways is a cutting-edge field that is attracting the attention of numerous industry players. Nonetheless, most of the targeted receptors currently belong to adaptive immunity , as is the case for ipilimumab.

Innate Pharma was founded in 1999 with the primary goal of targeting innate immune cells. It very quickly carved out a strong intellectual property portfolio on receptors in this category of the immune system. Over time, the Company has progressively become specialized in a type of drug - a tool for targeting innate immune cells: monoclonal antibodies (mAbs).

Innate Pharma's technological choice to focus on monoclonal antibodies corresponds to its intention to build on the experience accumulated with the anti-KIR programme (IPH21). It also reflects the history of this class of products, which has demonstrated – since the first ones on the market in the late 90s – a success rate (approval) greater than that obtained by chemical molecules (25% compared with about 11%, Carter, 2006) as well as being an extremely successful commercial venture.

<u>A market in excess of \$40Bn</u>

When the immune system detects an infectious agent or foreign body, it uses the B-lymphocytes to produce substances – known as antibodies – to fight it.



From antibodies to monoclonal antibodies (mAb)

Already used in the late 19th century in the form of antibody mixtures resulting from serums and plasma, antibodies became key therapeutic drugs in the 21st century thanks to advances made in biotechnologies. These technologies are used to grow cells to make them express certain proteins, something that conventional chemistry cannot achieve since proteins possess extremely complex structures. These cells are hence transformed into veritable mini biological factories. These technologies have made it possible to develop increasingly complex proteins (growth hormones, insulin, interferons, then antibodies and improved proteins). Improvements to these proteins have been successive: antibodies, for instance, were typically produced in rodents. These antibodies are now being humanized by replacing 'mouse' sequences with human sequences by means of genetic engineering. In this way, the side effects associated with their use can be minimized while optimizing their specific action



Antibodies are large proteins comprising two regions: a variable and a constant region. These two parts have different functions.

The variable part can recognize and specifically bind to some targets, then called antigens (cell receptor, circulating proteins,

The constant region has an effector function: it can block, destroy or activate the target.

I²: INNATE SCIENCE: mAb targeting innate immunity

Variable regions of antibodies are capable of recognizing an antigen and of binding with it. Simply by doing this, it can prevent the antigen from binding with its natural ligand.

As for the constant region, various actions and functions are possible when the antigen is carried by a cell: the destruction of the cell (by different means), the activation or inhibition of the cell, or the deposition of another drug (e.g. toxin) inside the cell. Depending on the targeted antigen, the antibody can be designed to perform any of these actions. For instance, Rituxan® kills the cell carrying the cancer marker in the lymphoma. In the case of several solid cancers, Avastin® binds blood vessels growth factor to prevent the blood vessels from growing and irrigating the developing tumor mass. Anti-TNF antibodies, such as Humira® or Remicade® which are used to treat chronic inflammatory pathologies like rheumatoid arthritis, recognize a pro-inflammatory molecule and neutralize it.

The teams at Innate Pharma are working on a new category of therapeutic antibodies: immunomodulating antibodies. These antibodies specifically recognize receptors on the immune cells with the purpose of activating them (in cancer therapy) or inhibiting them (for inflammatory diseases). Yervoy® is the first antibody to use this approach and gain approval. It recognizes a receptor of T-lymphocytes. The anti-KIR programme by Innate Pharma – licensed to Bristol-Myers Squibb – recognizes a receptor of NK cells and activates them against tumor cells. The anti-NKG2A programme – licensed to Novo Nordisk A/S – is designed to activate a sub-category of immune cells capable of regulating over-activated immune cells.



CO2 incubator "Kuhner" for the production of a few mg of antibody to be purified with a robot.



CYTOTOXIC ANTIBODIES

- The antibody binds to the target molecule on the tumor cell surface by its variable region and recruits different categories of killers by its constant region.
- 2. This binding provokes the destruction of the tumor cell by two mechanisms:
 - Lymphocytes that are recruited produce enzymes (in red) that • perforate the cell to which the antibody has bound *
 - The destruction by enzymes in the blood that are activated by the antibody itself ** (complement).
- 3. By secreting chemical signals called cytokines (in green), activated lymphocytes attract and activate surrounding immune cells so that they in turn contribute to the elimination of the tumor.
 - * ADCC, for Antibody-Dependent Cell-Mediated Cytotoxicity.
 - ** CDC, for Complement Dependent Cytotoxicity.



IMMUNOMODULATING ANTIBODIES IN INFLAMMATION

- Ι. The inflammatory response, useful in response to an attack (infection, injury) can sometimes become excessive or prolonged and can turn into a chronic inflammation.
- 2. Immunomodulating antibodies may act by different mechanisms to curb this pathological inflammation :
 - By blocking certain chemical messengers that drive the a) inflammatory reaction
 - By directly destroying or inhibiting overactive immune cells b)
 - c) By activating other immune cells which exert a regulatory role in inflammation

ANTIBODY-DRUG CONJUGATES IN CANCER



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IMMUNOMODULATING ANTIBODIES

The antibody binds by its variable end to a receptor present on a category of killer cells. Depending on the targeted receptor, the antibody blocks it (if it is an inhibitory receptor) or stimulates it (when it is an activating receptor). This leads in both cases to the activation of the corresponding killer cells.

Once activated, lymphocytes attack the tumor cells they have previously identified (not shown in this diagram) by binding and then perforating their membrane.

By secreting chemical signals called cytokines (in green), activated lymphocytes attract and activate surrounding immune cells so that they in turn contribute to the elimination of the



The antibody binds to a target molecule present on the surface of the tumor cell by its variable end while its constant end is coupled to a therapeutic agent (drug or radioactive isotope, for example).

In turn, the tumor cell internalizes the antibody conjugate which then releases the drug within the latter. The drug is activated and destroys the tumor cell from "inside," sparing the environment.