PRESS RELEASE

innate pharma

FOURTH CLINICAL TRIAL OPENED WITH MONALIZUMAB (IPH2201)

- ***Phase Ib/II trial testing monalizumab in combination with cetuximab in patients with relapsed or refractory head and neck cancer***
- ***Trial conducted in Europe and the United States***

Marseille, France, December 17, 2015

Innate Pharma SA (the "Company" - Euronext Paris: FR0010331421 – IPH) today announced the opening of the Phase Ib/II trial of monalizumab (previously IPH2201), a first-in-class NKG2A checkpoint inhibitor, in combination with cetuximab in patients with relapsed or metastatic squamous cell cancer of the head and neck (SCCHN). This multicentric trial, which will include up to 70 patients, will be performed in Europe and the United States. It is the second trial testing monalizumab in head and neck cancer, after the monotherapy neo-adjuvant trial opened in 2014.

Pierre Dodion, MD, Chief Medical Officer at Innate Pharma, said: "*HLA-E is frequently expressed by head and neck cancer cells. Monalizumab is a new checkpoint inhibitor targeting both T and NK cells and preventing their inhibition by HLA-E on tumor cells. Furthermore, monalizumab enhances antibody dependent cellular cytotoxicity (ADCC), one of the mechanisms of action of cetuximab, setting a sound rationale for their combination".* He added: *"All trials from Innate's initial clinical development plan are now recruiting patients, involving reference centers. We look forward to continuing on expanding this plan to fully explore the potential of monalizumab".*

Dr. Roger Cohen, Associate Director of Clinical Research at the Abramson Cancer Center and Professor of Medicine at the Hospital of the University of Pennsylvania, and lead investigator for the study, said: "*Cetuximab is the only targeted therapy approved in recurrent/metastatic head and neck cancer. However, its response rate of about 13% and response duration of less than 6 months leave a significant unmet medical need for this patient population. Immuno-oncology could play a key role in the treatment of head and neck cancer, as demonstrated by a variety of emerging and very promising data. The combination of monalizumab and cetuximab could enhance the efficacy of cetuximab by activating the immune system. This is a very appealing dual mechanism rationale".*

This trial is part of a global co-development and commercialization agreement with AstraZeneca for monalizumab. Within this framework, four Phase I/II trials are ongoing: the cetuximab combination trial in SCCHN, two single agent trials respectively in SCCHN and in ovarian cancer*, and a combination trial with ibrutinib in chronic lymphocytic leukemia. The co-development plan also includes a combination clinical trial with monalizumab and durvalumab (MEDI4736), a PD-L1 immune checkpoint inhibitor, in solid tumors, which will be performed by AstraZeneca/MedImmune.

* The trial in ovarian cancer is sponsored by NCIC Clinical Trials Group and performed in Canada.

About study IPH2201-203:

This Phase Ib/II study is a multicenter open label trial of the combination of monalizumab and cetuximab in patients with recurrent or metastatic SCCHN. Both HPV positive and negative patients will be included.

The study objectives are to assess the safety and antitumor activity of the combination of monalizumab and cetuximab. The primary endpoint for efficacy is overall response rate. The trial will be performed in Europe and in the United States.

Seventy patients maximum are planned to be enrolled. The trial will be conducted in two parts:

- In the first part of the study, up to 30 patients will receive a combination of cetuximab and monalizumab; 5 dose levels of monalizumab up to 10 mg/kg will be explored. Based on previous experience with monalizumab, these dosages are expected to induce full saturation of the NKG2A receptor;
- In the second part of the study, monalizumab will be assessed at the dose selected in the dose-escalating part, in combination with cetuximab, in 40 patients who received up to 2 prior systemic regimens. Treatment will be continued until progression or unacceptable toxicity.

The rationale of this trial is based on the observation that HLA-E is expressed on tumor cells in 78% to 86% of patients with SCCHN[†‡]. Among 150 patients with tonsillar SCC, overexpression of HLA-E was found in 99/119 (83%) of those with HPV- tumors and 30/31 (97%) with HPV+ tumors[‡]. HLA-E is a ligand of the inhibitory CD94/NKG2A receptors that are found on Natural Killer (NK) cells and intratumoral $CD8^+$ T cells in a variety of tumor types, including SCCHN[§]. Upon binding to NGK2A, monalizumab restores the capability of those cells to destroy tumor cells.

Cetuximab is an anti-EGFR monoclonal antibody acting through blocking oncogenic signaling and by antibody dependent cellular cytotoxicity (ADCC), a mechanism mediated by NK cells. Furthermore, cetuximab-mediated ADCC is inhibited by HLA-E expression and this inhibition can be circumvented with anti-NKG2A treatment[**].

About head and neck cancer:

SCCHN is estimated to be the sixth most common cancer worldwide with 650,000 cases and 200,000 deaths per year worldwide, and the most common cancer in Asia. They usually begin in the squamous cells that line the moist, mucosal surfaces inside the head and neck (for example, inside the mouth, the nose, and the throat).

When metastatic at presentation or recurrent and/or metastatic after initial treatment, SCCHN is usually an incurable disease. These patients have a short life expectancy and treatment options are limited. Cetuximab is approved by the FDA and the EMA for the treatment of patients with incurable recurrent and/or metastatic SCCHN.

Cetuximab prolongs survival when added to radiation therapy in loco-regionally advanced SCCHN (Bonner, Harari et al. 2006) and when added to platinum-based chemotherapy as first-

[†] Silva, Crispim et al. 2011
[‡] Nasman, Andersson et al. 2013
[§] Braud, Allan et al. 1998; Lee, Llano et al. 1998; Gooden, Lampen et al. 2011; Katou, Ohtani et al. 2007
[**] Levy, Sycz et al. 2009

line treatment for recurrent or metastatic SCCHN (Vermorken, Mesia et al. 2008). However, as a single agent in disease refractory to platinum-based therapy, cetuximab yields only modest antitumor activity with a response rate of 13%, a median time to progression of 70 days and a median survival of 178 days (Vermorken, Trigo et al. 2007). A subsequent randomized trial of single agent cetuximab versus afatinib in platinum-based therapy failures yielded an overall response rate of 9.7% and a progression-free survival of 15 weeks for the patients treated with cetuximab (Seiwert, Fayette et al. 2014).

In a preliminary study of durvalumab, a PDL-1 inhibitor, 62 patients were enrolled with a median of 3 prior treatments, and overall response rate of 11% (7/62) was achieved with an 18% response rate (4/22) in the PDL-1 positive subgroup (Segal and al. 2015). Clinical studies with other checkpoint inhibitors are ongoing or have shown response rates of interest in SCCHN.

New treatment options are therefore needed to address the high unmet medical need of patient with recurrent and/or metastatic SCCHN.

About monalizumab (IPH2201):

Monalizumab is a first-in-class immune checkpoint inhibitor targeting NKG2A receptors expressed on tumor infiltrating cytotoxic CD8 T lymphocytes and NK cells.

NKG2A is an inhibitory receptor binding HLA-E. By expressing HLA-E, cancer cells can protect themselves from killing by NKG2A$^+$ immune cells. HLA-E is frequently up-regulated on cancer cells of many solid tumors or hematological malignancies. Monalizumab, a humanized IgG4, blocks the binding of NKG2A to HLA-E allowing activation of NK and cytotoxic T cell responses. Hence, monalizumab may re-establish a broad anti-tumor response mediated by NK and T cells. Monalizumab may also enhance the cytotoxic potential of other therapeutic antibodies.

Monalizumab is partnered with AstraZeneca and MedImmune, AstraZeneca's global biologics research and development arm, through a co-development and commercialization agreement. The initial development plan includes: Phase II combination clinical trial with durvalumab (MEDI4736) in solid tumors; multiple Phase II trials planned by Innate Pharma to study monalizumab both as monotherapy and in combination with currently approved treatments across a range of cancers; and the development of associated biomarkers. As previously announced, under the terms of this agreement, Innate Pharma is eligible to cash payments of up to $1.275 billion as well as double digit royalties on sales. In addition to the initial payment of $250 million to Innate Pharma, AstraZeneca will pay a further $100 million prior to initiation of Phase III development, as well as additional regulatory and sales-related milestones of up to $925 million. AstraZeneca will book all sales and will pay Innate Pharma double-digit royalties on net sales. The arrangement includes the right for Innate Pharma to co-promote in Europe for a 50% profit share in the territory.

About Innate Pharma:

Innate Pharma S.A. is a biopharmaceutical company discovering and developing first-in-class therapeutic antibodies for the treatment of cancer and inflammatory diseases.

The Company has three clinical-stage programs, including two checkpoint inhibitors in immuno-oncology, a new therapeutic field that is changing cancer treatment by enhancing the capability of the body's own immune cells to recognize and kill cancer cells.

Its innovative approach has translated into major alliances with leaders in the biopharmaceutical industry such as Novo Nordisk A/S, Bristol-Myers Squibb and AstraZeneca.

Listed on Euronext-Paris, Innate Pharma is based in Marseille, France, and had 112 employees at September 30, 2015.

Learn more about Innate Pharma at www.innate-pharma.com.

Practical Information about Innate Pharma shares:

ISIN code	FR0010331421
Ticker code	IPH

Disclaimer:

This press release contains certain forward-looking statements. Although the company believes its expectations are based on reasonable assumptions, these forward-looking statements are subject to numerous risks and uncertainties, which could cause actual results to differ materially from those anticipated. For a discussion of risks and uncertainties which could cause the company's actual results, financial condition, performance or achievements to differ from those contained in the forward-looking statements, please refer to the Risk Factors ("Facteurs de Risque") section of the *Document de Reference* prospectus filed with the AMF, which is available on the AMF website or on Innate Pharma's website.

This press release and the information contained herein do not constitute an offer to sell or a solicitation of an offer to buy or subscribe to shares in Innate Pharma in any country.

For additional information, please contact:

Innate Pharma

Laure-Hélène Mercier
Director, Investor Relations

Tel.: +33 (0)4 30 30 30 87
investors@innate-pharma.com

ATCG Press
Marie Puvieux (France)
Mob: +33 (0)6 10 54 36 72
Jean-Medhi Grangeon (ROW)
Mob: +33 (0)6 62 22 00 24
presse@atcg-partners.com