# PRESS RELEASE

innate pharma

## INNATE PHARMA PRESENTS ENCOURAGING DATA ON ITS IMMUNOMODULATORY PRODUCT CANDIDATE IPH 1101 WITH FINAL RESULTS FROM PHASE I CLINICAL TRIAL IN SOLID TUMOURS (TRIAL D004-101)

**Marseilles, France, September 6, 2006**

Innate Pharma S.A. (www.innate-pharma.com), a biopharmaceutical company specialized in immunology and developing new drug classes targeting innate immunity, with an initial focus in cancer, announced today encouraging clinical data results for the development of IPH 1101 (bromohydrin pyrophosphate - BrHPP, a phosphorylated NCE), the company's most advanced product of its gamma-delta T ($\gamma\delta$ T) platform.

The T$\gamma\delta$ platform - one of Innate Pharma's three product platforms currently under development - is formed by a family of chemically-synthesized, structural analogs of non-conventional antigens which specifically activate the V$\gamma$9V$\delta$2 T-lymphocytes subset. IPH 1101, one of the platform's products, has been developed for intravenous delivery in association with subcutaneous, low-dose Interleukin 2 (IL-2). IPH 1101 potentiates the direct cytotoxic activity of $\gamma$9$\delta$2 T cells against a large number of tumour cell lines (including renal carcinomas), and also triggers the synthesis of pro-inflammatory cytokines - inducing the recruitment of other cell effectors and facilitating implementation of an adaptive response.

The drug candidate has completed a Phase I trial in solid tumours and metastatic renal carcinoma (mRCC). The final results of this study (trial D004-101) are now available and have been submitted for presentation at the next 11$^{th}$ ICDT Conference on Innovative Therapeutics in Oncology, to be held this fall, November 4-8, in Versailles, France.

In 2004, IPH 1101 was granted orphan drug status by the EMEA (the European Medicines Evaluation Agency) for treatment of metastatic renal carcinoma (mRCC).

### About IPH 1101 phase I clinical trial in solid tumours (trial D004-101):

The Phase I trial was an open-label, dose-escalation study, which was conducted at two centres in France in sequential cohorts of patients with advanced/metastatic solid tumours. The primary objective was to define the safety profile when IPH 1101 is administered alone and in combination with Aldesleukin, to determine the maximum tolerated dose (MTD), the dose-limiting toxicity (DLT), and the recommended dose of IPH 1101 to be used for further development in combination with a fixed low s.c. dose of Aldesleukin. The secondary objectives were to evaluate pharmacokinetic and pharmacodynamic parameters, and to document any anti-tumour activity.

Eligible patients were treated with successive administrations of IPH 1101 (alone and in combination with Aldesleukin). IPH 1101 was administered i.v. alone for the first cycle, and in combination with Aldesleukin for the subsequent cycles. Patients were to be sequentially assigned to cohorts at progressively higher dose levels of IPH 1101.

**A total of 28 patients with various solid tumours have been treated in the study including 18 patients with mRCC.**

**In terms of safety**, **the product has been well tolerated** with main Adverse Events being transient signs of cytokine release (fever, hypotension, nausea). Most of these adverse events were only observed at the first administration of IPH 1101 alone, and were of less intensity in subsequent cycles, with co-treatment of Aldesleukin. Two patients experienced dose limiting toxicities at 1800 mg/m² - one patient had fever and hypertension (CTC* grade 3) and the other had hypotension (CTC grade 3) - leading to confirm good tolerance and safety of a lower dose of 1500 mg/m², tested on 10 patients and which has been considered as the Maximum Tolerated Dose as well as the recommended dose for further development.

**In terms of biological activity**, this phase I clinical trial provides a further evidence of the specific and reproducible pharmacological activity of IPH 1101 toward human γδ cytotoxic T cells. Among the 25 evaluable patients for pharmacodynamic evaluation, 21 patients showed a **significant increase of their circulating γδ T cells**, evaluated by dedicated flow cytometry analysis. In parallel, no other immune cell type (NK, T cells) showed any amplification, demonstrating **the specific targeting of the γδ population**. The γδ T cell amplification correlated with IPH 1101 dose. In the highest dose-groups, 4 patients (including 3 mRCC), showed γδ T cell increases ranging from 50 to 240 times the basal values. **In most patients, IPH 1101 also induced early release of immunomodulatory and antitumoral soluble factors**, such as INFg, MIP1a, IL-8, IL-6, MCP-1 and TNFα.

**In terms of clinical activity**, tumour evaluations performed in the 15 mRCC patients evaluable for efficacy (out of 18 mRCC patients treated) showed a **disease stabilisation of more than 35 weeks for 8 patients out of 15**. These *in vivo* data, which confirmed the data generated *ex vivo* with IPH 1101 (in a cellular therapy setting) and published at ASCO in June 2006, are encouraging signals in such an advanced kidney cancer patient population, supporting further evaluation in this indication with the ongoing randomised Phase II in mRCC patients.

*"These Phase I results, and notably the clinical activity data, which where not the primary objective of the trial, are very encouraging results for moving forward our γδ T platform into full development,"* stated Hervé Brailly, Innate Pharma's CEO. *"They indicate a promising potential in oncology for IPH 1101. In metastatic renal carcinoma, we are convinced that immunotherapy will play an important role in the management of the disease, complementing the newly approved TKIs. We are going to further explore the potential of IPH1101 in oncology, through the ongoing randomized Phase II in mRCC, and with an aggressive plan for several additional Phase II trials to be initiated in the short run".*

* *Common Toxicity Criteria*

## About other ongoing or planned trials with IPH 1101:

Another multi centric Phase I study is ongoing in Non-Hodgkin's Lymphoma (trial D004-102). A multi-centric randomised Phase II clinical trial has started in metastatic Renal Cell Carcinoma in France, Russia and Ukraine (trial D004-201). Patient recruitment is ongoing in the 15 clinical centres. 68 patients are expected to be treated in this trial and clinical activity data should be available for the end of 2007. Innate Pharma plans to have a total of four Phase II trials ongoing in cancer in 2007. The product has also been used as an adoptive, autologous immunotherapy procedure designed to produce large numbers of highly-enriched $T\gamma 9\delta 2$ cells from a patient's blood sample, and where peripheral lymphocytes are harvested by leukapheresis and cultured in the presence of IPH 1101 and IL-2, prior to re-infusion into the bloodstream (trial D001-101). Positive data on this approach from a phase I clinical trial in mRCC patients were presented last summer at the 2006 ASCO Annual Meeting and are available on the Company's website.

## About Innate Pharma:

Founded in 1999, Innate Pharma S.A. is a biopharmaceutical company in clinical stage, developing First in class[†] drug candidates targeting the innate immune system. The pioneering work of Innate Pharma's scientific founders and its team led to three product platforms – each indirectly validated in clinical settings in oncology. Taking into account their mechanisms of action, Innate Pharma's drug candidates also present a potential development outside oncology, particularly in the control of viral infections and chronic inflammation related to auto-immune pathologies. As a result of its scientific position in innate immunity pharmacology, its intellectual property portfolio and its know-how in R&D, Innate Pharma aims to become a leader in the rapidly growing market of immunotherapy.
Innate Pharma has raised approximately 50 million euros in three VC rounds of financing (2000, 2002, and 2004) as well as a reserved capital increase for its partner, Novo Nordisk A/S, in a deal closed on March 29, 2006. In addition to Novo Nordisk A/S, investors in Innate Pharma are reference biotechnology investors, including: Sofinnova Partners (France), Alta Partners (USA), GIMV (Belgium), Auriga Partners (France), Inserm-Transfert (France), Gilde Healthcare (the Netherlands), Pechel Industries (France), Innoveris (France), NIF (Japan), and Quilvest (France). Based in Marseilles, France, Innate Pharma's R&D activities are ISO 9001:2000 certified (since 2005).
As of August 31, 2006, Innate Pharma had 66 employees, including 16 Doctors in Science, Medicine and Pharmacy. More than 70% of Innate Pharma's staff is involved in R&D activities.

**Press and Analyst Contacts:**

**Innate Pharma**
Stéphane Boissel, CFO
Tel: (+33) 4 96 19 05 58
stephane.boissel@innate-pharma.fr

**Alize PR**
Caroline Carmagnol
Tel: (+33) 6 64 18 99 59
caroline.carmagnol@wanadoo.fr

**For information about clinical trials:**
Patrick Squiban, MD, CMO
Tel: (+33) 4 96 19 05 42
patrick.squiban@innate-pharma.fr

[†] *with new mechanisms of action*