

# IPH1101-202

## interim results

A phase I/II open label study of IPH1101  
(with low dose of IL-2)  
in combination with rituximab re-treatment  
in patients with Follicular Lymphoma





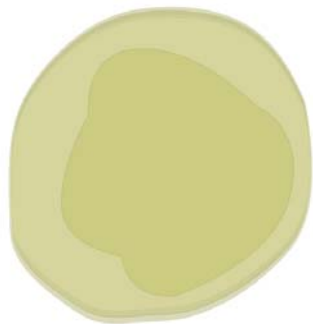
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# IPH1101-202 interim results

Summary of data presented at the ECCO/ESMO  
Congress in Berlin, September 21, 2009

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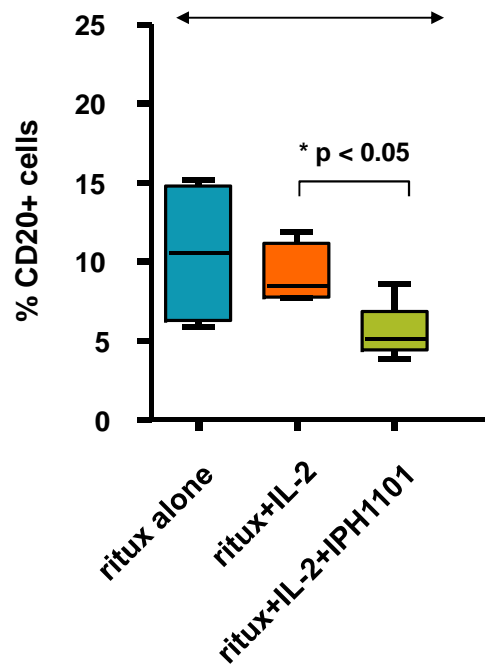


# IPH 1101-202 – Follicular non Hodgkin's Lymphoma

## Study rationale

- Scientific rationale for  $\gamma\delta$  therapy in B-NHL treatment
- Strong preclinical data suggesting synergy between activated  $\gamma\delta$  and rituximab
- Rituximab re-treatment gives:  
40% ORR (overall response rate)  
and about 10% CRR (complete response rate)  
(Davis et al.; JCO 2000)

**B-cell depletion in lymphoid organs at End of Study in the primate**

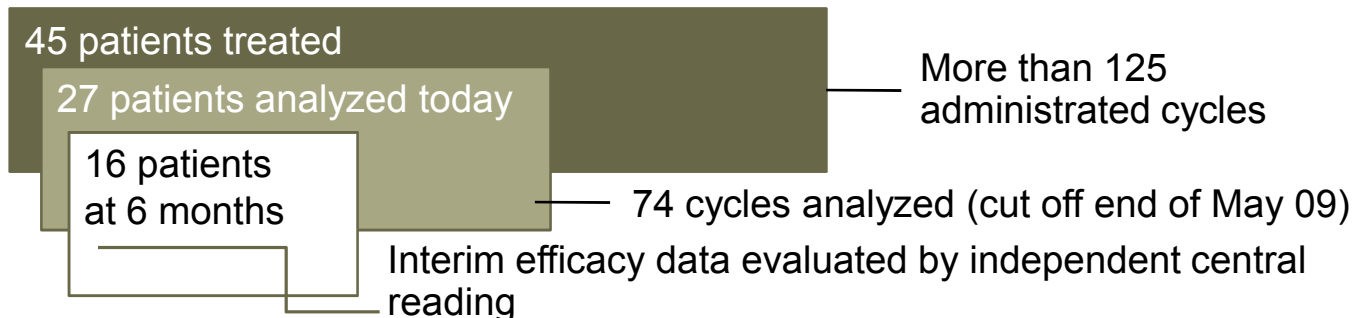




# IPH 1101-202 – Follicular non Hodgkin's Lymphoma

## Protocol reminder

- Phase I/II multicenter study
- FL Patients grade 1 or 2 (WHO) relapsing after up to 4 lines of treatment, at least one containing rituximab
- 3 courses of IPH1101 (750 mg/m<sup>2</sup>, 30-min i.v. infusion) 3 weeks apart in association with IL-2 (2 M IU daily for 5 days) + rituximab
- Primary endpoint: overall response rate (partial and complete response, Cheson criteria)
- Secondary endpoints: safety, biological activity of the combination, biological activity / clinical efficacy relationship



**Preliminary results presented today at ESMO**



# IPH 1101-202 – Follicular non Hodgkin’s Lymphoma

Population – 27 patients

<b>Age</b>	Median Range > 50 years old	57 39-73 67%
<b>Sex (M/F)</b>		14/13
<b>ECOG*</b> * Scale of disease severity. The higher the ECOG, the poorer the prognosis	0 1	85% 15%
<b>FLIPI*</b> * Follicular Lymphoma International Prognostic Index. The higher, the poorer	Low Intermediate High (Poor)	70% 15% 15%
<b>High LDH</b>		37%
<b>Prior lines of treatment</b>	One line Two to four lines	60% 40%
<b>Mediastinal or intra abdominal involvement*</b> * Deep ganglions involvement: marker of severity of the disease	Yes No	70% 30%
<b>Median time since last treatment</b>		20 months

**Overall population is comparable to the reference paper population**



## Safety data

- 27 patients
  - Most patients had a good tolerance with a report of toxicity of grade 1 or 2
  - Main adverse events are related to cytokine release (fever, chills, nausea)
- 45 patients:
  - 9 patients experienced possibly or probably related SAEs
  - 4 patients withdrew from study for toxicity events

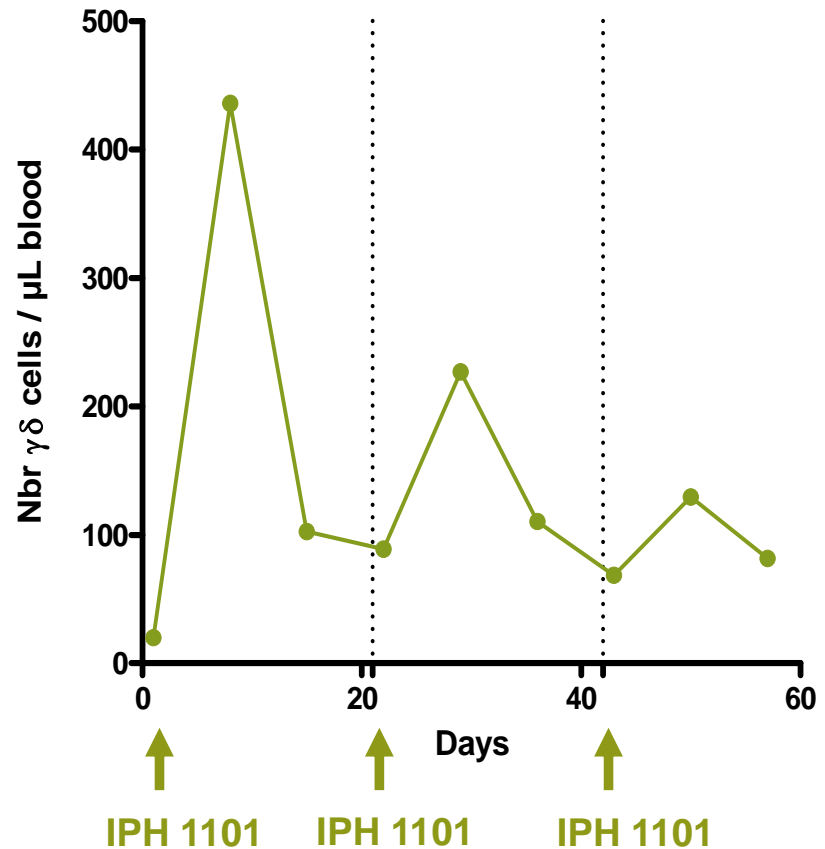
**Satisfactory and manageable overall tolerance and safety**



# IPH 1101-202 – Follicular non Hodgkin’s Lymphoma

## Pharmacodynamic data – 27 patients

- IPH 1101 + IL-2 low dose enable expansion of  $\gamma\delta$  T cell population at each cycle

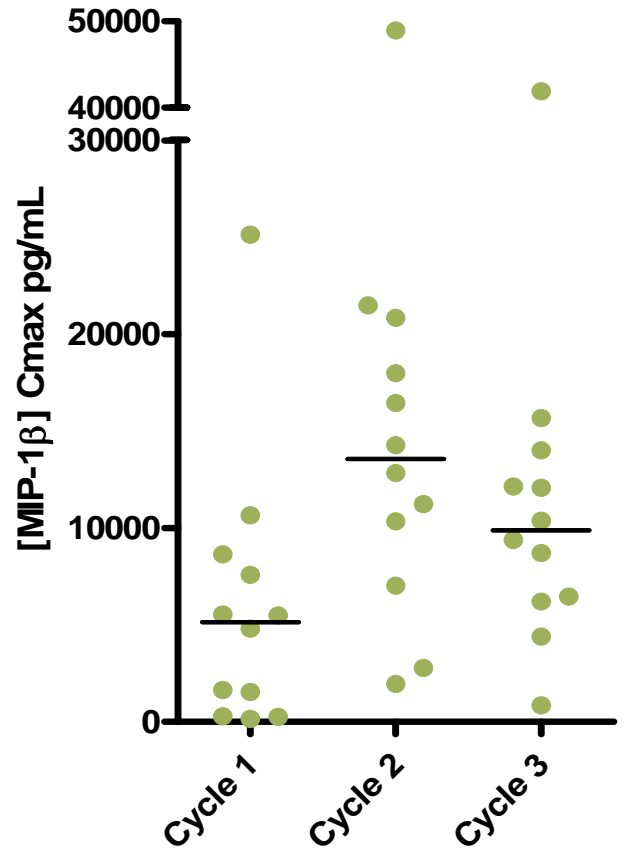




# IPH 1101-202 – Follicular non Hodgkin’s Lymphoma

## Pharmacodynamic data – 27 patients

- Strong cytokines release at each cycle of IPH 1101
  - Cytokines directly produced by  $\gamma\delta$  T cells:  $\text{INF}\gamma$ ,  $\text{TNF}\alpha$ ,  $\text{MIP1}\beta$
  - Cytokines produced through by-stander effect:  $\text{IL-6}$ ,  $\text{MCP1}$





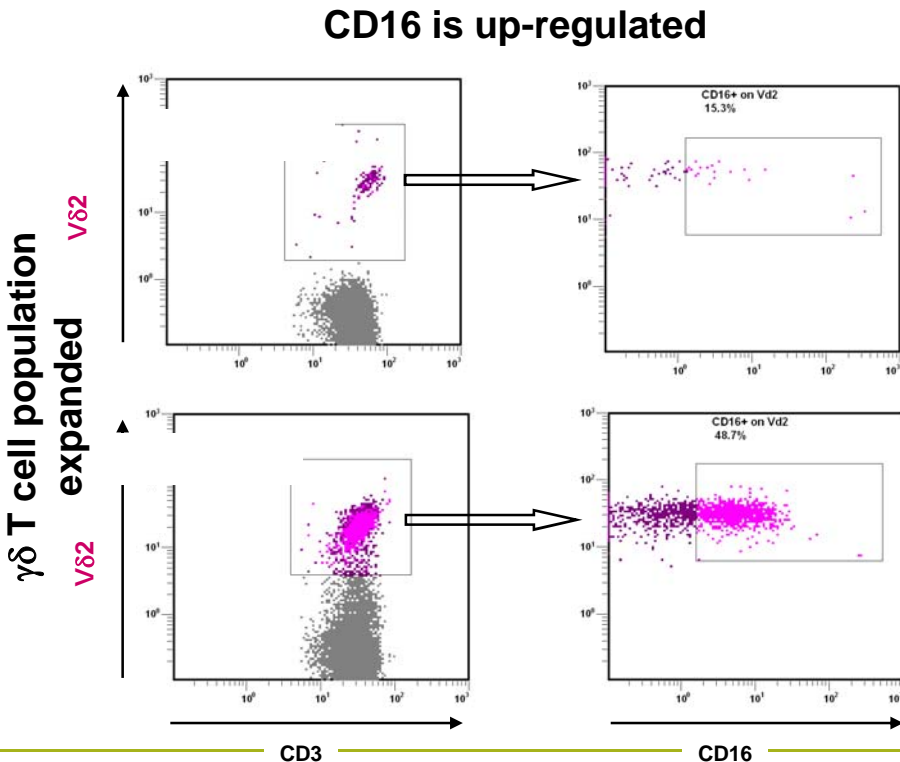
# IPH 1101-202 – Follicular non Hodgkin’s Lymphoma

## Pharmacodynamic data – 27 patients

- Up-regulation of CD16 receptor on  $\gamma\delta$  T cells: substantiate potential synergy between IPH 1101 and rituximab

Pre-dose  $\gamma\delta$  represent 1.5% among T cells and 15.3% of  $\gamma\delta$  T cells express CD16

At the last assesment (15 days after 3rd cycle),  $\gamma\delta$  represent 14.1% among T cells and 48.7% of  $\gamma\delta$  T cells express CD16





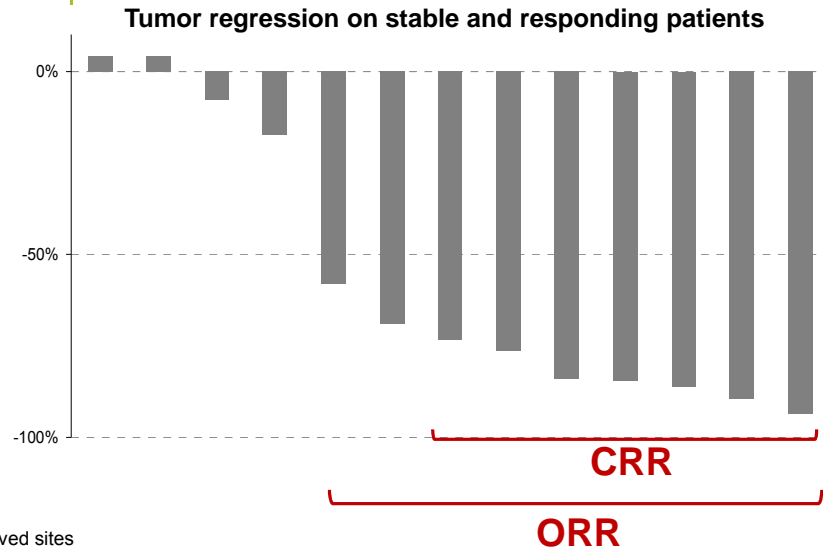
# IPH 1101-202 – Follicular non Hodgkin’s Lymphoma

## Efficacy data – 16 patients, independent central evaluation

Complete Response	5
Undetermined Complete Response	2
Partial Response	2
Stable Disease	4
Progressive Disease	3

**CRR:**  
**44%**

**ORR:**  
**56%**



Based on Cheson criteria (*Cheson et al., JCO, 1999*)

CR: diminution of >75% of total lesion size and no bone marrow involvement

CRu: diminution of >75% of total lesion size without bone marrow assessment

PR: diminution of >50% of total lesion size

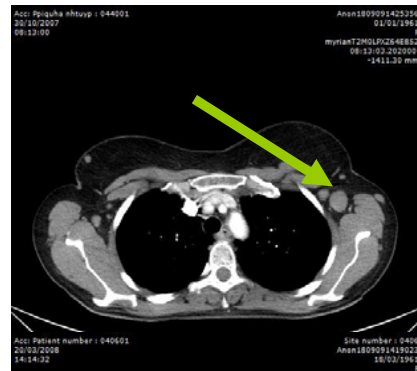
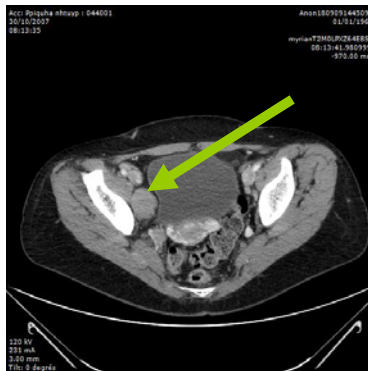
SD: less than a PR but not progressive disease

PD: appearance of a new lesion or increase of  $\geq 50\%$  in the size of previous involved sites

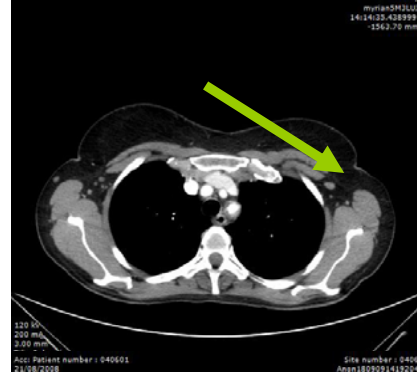
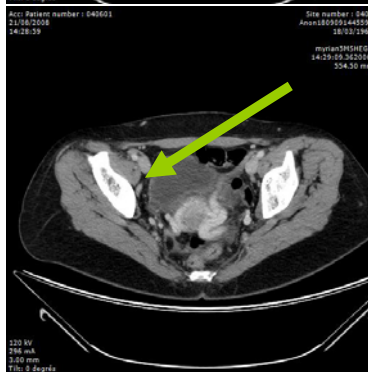
# IPH 1101-202 – Follicular non Hodgkin's Lymphoma Case study

- Patient aged 46, high LDH, poor FLIPI
- Treated with R-CHOP 20 months before, best response PR
- In CR with IPH 1101 + R - Still in CR after 22 months.

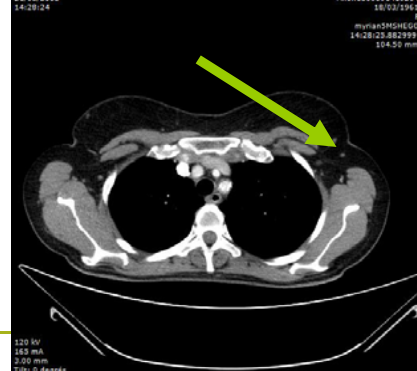
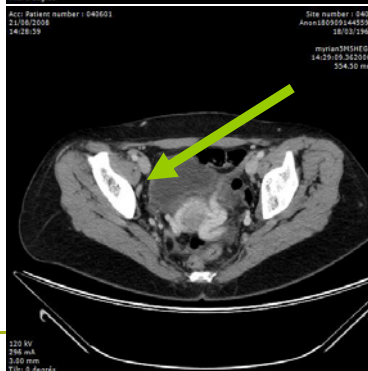
Baseline



5 mo



10 mo





# Conclusions

To date, data at 6 months for 16 patients have been assessed by the independent central review

- Encouraging rate of response with high rate of CR seen in first set of 16 patients
  - Known to be related to response duration
  - Reference paper Davis et al. (*JCO, 2000*): 40% ORR and about 10% CRR expected in this population
- Satisfactory and manageable overall tolerance and safety
- Pharmacological activity validating the synergistic effect of IPH 1101 on  $\gamma\delta$  T cells when administered in combination with rituximab
- Enhancement of the effector function of  $\gamma\delta$  T cells in combination with a cytotoxic antibody could have a significant clinical impact in the disease treatment



*Perspective  
Innate Pharma going forward  
Hervé Brailly, CEO of Innate Pharma*

- IPH 1101 has a new mechanism of action that might have a significant impact in cancer treatment in combination with cytotoxic antibodies
  - Enhancement of Antibody-Dependent Cellular Cytotoxicity (ADCC)
  - Direct cytotoxic activity
- Strong medical need in NHL to improve quality of response, duration of response and to treat relapsing / refractory patients
  - Rituxan to remain a core component of disease management
  - IPH1101 could be combined with other cytotoxic MAb
- Future envisaged positioning for IPH1101 could be in combination with rituximab in first line patients with indolent, small mass fNHL eligible to rituximab-alone therapy
- Enrolment completed – Final data by mid-2010



## Oncology

<b>Monotherapy</b>	<b>2<sup>nd</sup> line, metastatic</b>	<b>mRCC</b>	<b>Data published in 2Q08, good results on <math>\gamma\delta</math> pharmacodynamics, primary efficacy endpoint not reached</b>
<b>Combination</b>	<b>Relapse after at least one line of treatment including rituximab</b>	<b>fNHL Combination with rituximab</b>	Encouraging preliminary data Final data 1Q 2010
	<b>Residual disease</b>	<b>CML Combination with imatinib</b>	<b>Good results on <math>\gamma\delta</math> pharmacodynamics, primary efficacy endpoint not reached</b>

## Infectious diseases

<b>Monotherapy</b>	<b>1<sup>st</sup> line</b>	<b>HCV</b>	Data published on 2Q09 Primary endpoint reached First proof of concept in patients of $\gamma\delta$ T cell activation anti-viral effect
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# Innate Pharma moving ahead

## Strategic priorities 2009-2011

- ▶ Achieve proof of concept with IPH immunotherapy approach
  - ⇒ Complete Phase II program with IPH 1101 to obtain clinical POC in 2009
  - ⇒ Begin Phase II program with IPH 2101 to obtain clinical POC in 2011
  
- ▶ Business development
  - ⇒ To accelerate the development and commercialization of IPH drugs
  - ⇒ To secure additional financing
  
- ▶ Feed clinical portfolio with innovative drug candidates
  - ⇒ Target beyond innate immunity, build on mAb development know-how



# Innate Pharma moving ahead

## Recent achievements and perspective

- IPH1101 Phase II program near completion
  - Recruitment completed in all trials
  - Preliminary encouraging data in NHL
  - Positive data in HCV
  - No plan to invest in late-stage development
  - Final data of Phase II program will open window for partnering
- In-house resources focused on development of antibodies
  - Start of first Phase II with IPH 2101
  - Strong commitment to IPH 4201
  - Partnership with Inserm to feed R&D with innovative early targets



# Innate Pharma

## Investment case

- A unique access to novel targets
  - To develop first-in-class drug candidates
- A productive R&D platform
  - Rich and diversified pipeline
  - Moderate cash burn
  - Credible partner for pharma companies
- 2009 value inflexion
  - Phase II POC data with most advanced program
  - Second program in Phase II
- Cash into 2011
  - Next value inflexion with Phase II POC data with most advanced antibody program

 Turning novel targets into first-in-class immunotherapeutics

# Pipeline status

Broad and diversified portfolio, primary focus on cancer

Candidate	Target	M0	M1	M2	M3	2009 expected news flow
		Validation	Preclinical	Phase I	Phase II	
IPH 1101/ IPH 1201	γδ TCR	Follicular lymphoma / fNHL			Phase II	<ul style="list-style-type: none"> <li>Phase II data ✓</li> <li>Phase II final results in 2010</li> </ul>
		Chronic myeloid leukemia / CML				
		Type C hepatitis / HCV				
IPH 2101	KIR2DL1,2,3	Multiple myeloma / Mmy			Phase II	<ul style="list-style-type: none"> <li>Phase I data ✓</li> <li>Start Phase II ✓</li> </ul>
		Acute myeloid leukemia / AML				
IPH 2201 (NN8765)	undisclosed	Inflammation, autoimmunity			<ul style="list-style-type: none"> <li>Out-licensed</li> </ul>	
IPH 24	undisclosed	Inflammation, autoimmunity				
IPH 4101	KIR3DL2	CTCL			<ul style="list-style-type: none"> <li>Opportunities for early-stage collaborations</li> <li>R&amp;D fueling the pipe</li> </ul>	
IPH 4201	FAPP/BSDL	Pancreatic cancer				
IPH 3102	TLR3	Cancer				
IPH 3201	TLR7/8	Vaccine adjuvant				





# CONTACTS

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