innate pharma

COMPANY PRESENTATION

1Q2016

IPH LISTED NYSE EURONEXT

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FORWARD LOOKING STATEMENT

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This document contains data pertaining to the Company's potential markets and the industry and environment in which it operates. Some of these data comes from external sources that are recognized in the field or from Company's estimates based on such sources.

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Please refer to the Document de Référence filed with the Autorité des marchés financiers ("AMF") on March 12, 2015, available on the AMF's website (www.amf-france.org) and on the Company's website (www.innate-pharma.com). Such documents may not be necessarily up to date.

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INNATE PHARMA AT A GLANCE

Portfolio of first-in-class checkpoint inhibitors

Differentiated science in Immuno-Oncology

innate pharma

Partnerships with BMS, AZN, Sanofi

Innovative ADC and bispecific antibody technologies

2015: CREATING THE PLATFORM FOR GROWTH

- **Strengthening the base**
  - > Landmark co-development and commercialization agreement with AstraZeneca for monalizumab in immuno-oncology
  - > Initial clinical program of 5 trials implemented
- **Building foundations for future growth**
  - > IPH4102 in clinical development
  - > New first-in-class anti-CD39 checkpoint inhibitor program, IPH entry to tumor microenvironment checkpoint inhibition
  - > New bispecific NK cell engagers technology and research collaboration and licensing agreement with Sanofi
- **Staffing for growth**
  - > 19 new FTEs mostly in wetlab and clinical operations
  - > 118 employees at end of year
- **Strong balance sheet**
  - > Cash and cash equivalents and financial instruments amounting to €274 million at end of year

LONG TERM STRATEGY

MOVING TOWARDS AN INTEGRATED BIOPHARMA COMPANY

R&D collaboration

2003 - 2009

novo nordisk®

Global co-development and commercialization

2015

Monalizumab (PII)

AstraZeneca MedImmune

1999

Inception

2010

License

2011

Lirilumab (PII)

Bristol-Myers Squibb

2015

2020

Expansion of proprietary pipeline

- **IPH4102** in house development
- In-licensing of **anti-CD39** program
- Development of **proprietary technologies** (ADC, bispecifics)

THREE PILLARS OF DEVELOPMENTS

CLINICAL PIPELINE

- 2 broad potential checkpoint inhibitors partnered with leaders in IO currently in Phase II
- 1 Phase I proprietary cytotoxic mAb

PRECLINICAL PIPELINE

- Core focus in innate receptor pharmacology
- Targeting T and NK effector cells and beyond

INNOVATIVE TECHNOLOGIES

- Novel formats
- Non-exclusive partnerships

- Supported by a strong cash position

INNATE PHARMA PIPELINE

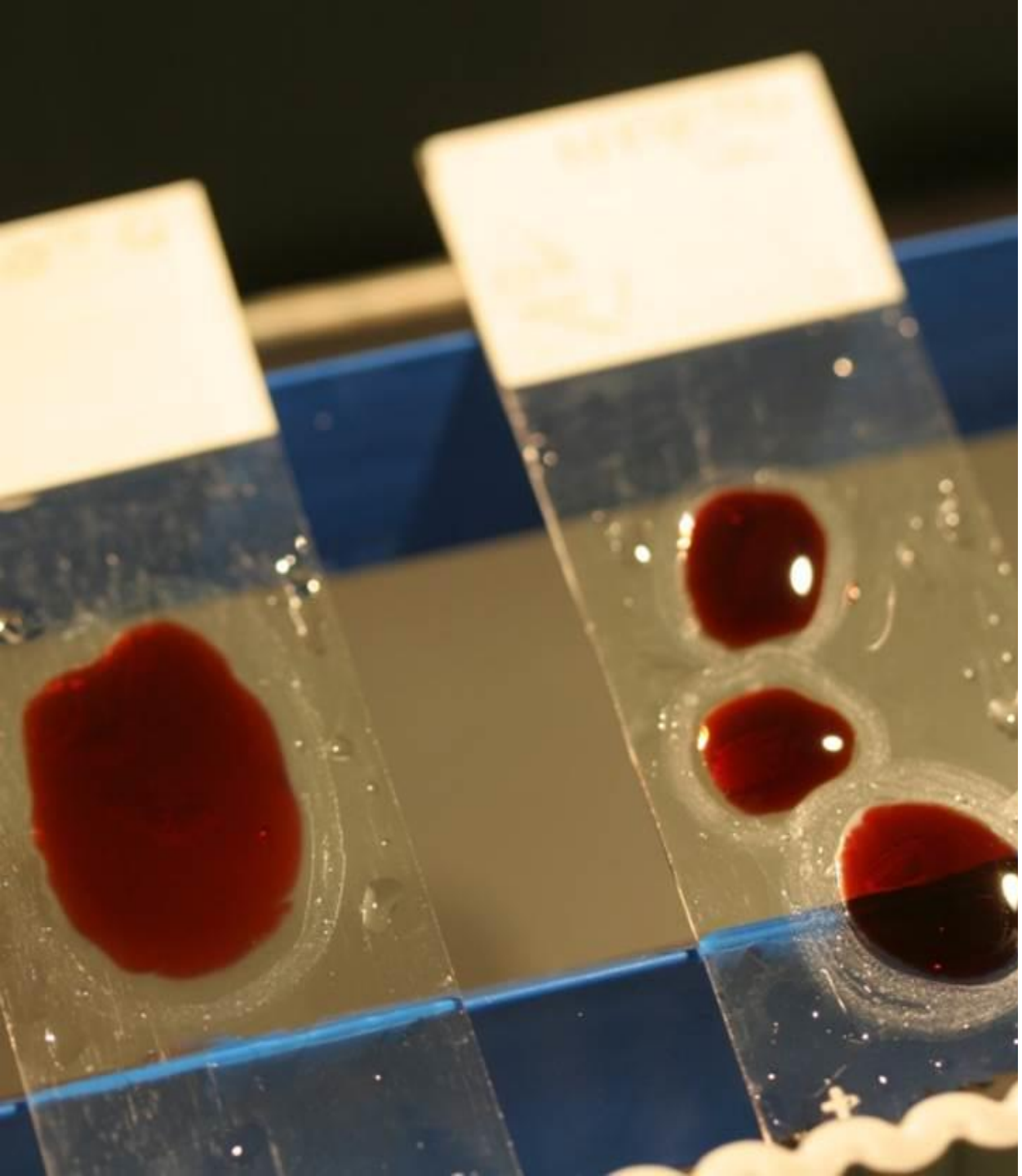
PROGRAM	TARGET	INDICATION	STAGE
Lirilumab License to Bristol-Myers Squibb	KIR2DL1,2,3	Acute Myeloid Leukemia - Single agent Solid & heme tumors - Multiple combinations	Phase IIb 6 Phase I & II trials
Monalizumab Co-development with AstraZeneca	NKG2A	Solid & heme tumors - Single agent and multiple combinations	5 Phase I/II trials
IPH4102	KIR3DL2	Cutaneous T-cell lymphomas	Phase I
IPH43	MICA	Cancer	Research
Discovery	CD39	Cancer	Research
IPH33	TLR3	Inflammation	Research

TECHNOLOGY	COLLABORATIONS
NK bispecific engagers	Sanofi
Antibody Drug Conjugate (ADC)	

EXPECTED NEWSFLOW IN 2016-2017

PROGRAM	MAIN NEWS 2015	NEXT STEPS
Lirilumab License to Bristol-Myers Squibb	Effikir & combination in solid tumors on track 5 new combination trials in heme malignancies	**Start of clinical trials read-out in 2016**
Monalizumab Co-development with AstraZeneca	5 Phase I/II trials roll out	**First data in 2017** **Broadening of clinical program**
IPH4102	EU/US Phase I started in 2015	**Clinical data expected end of 2017/2018**
IPH43		**Regulatory preclinical development**
Discovery anti-CD39	In-licensing	**Lead selection**
IPH33		**Candidate for out-licensing**

TECHNOLOGY	MAINS NEWS 2015
NK bispecific engagers	Research and licensing agreement for new bispecific antibodies with Sanofi
Antibody Drug Conjugate (ADC)	

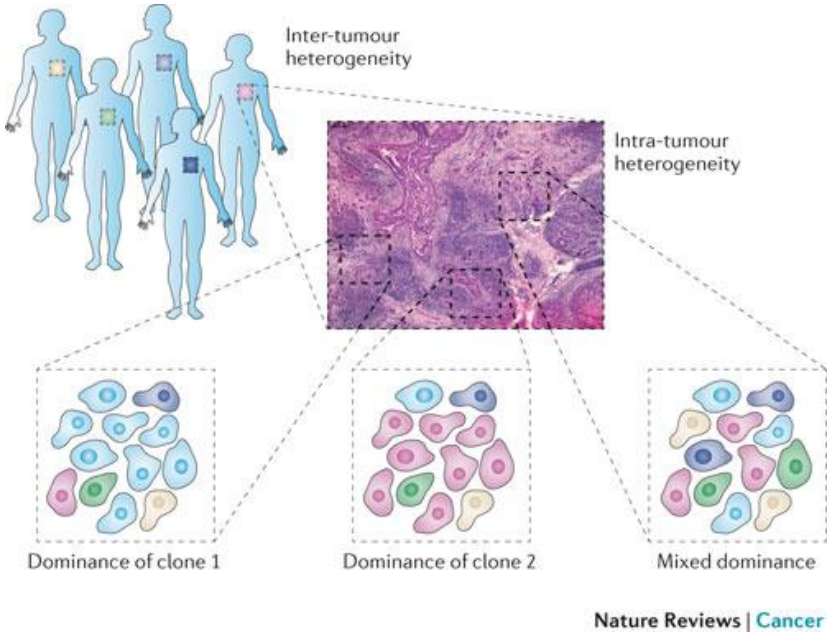


TARGETING NK CELLS AS A THERAPEUTIC APPROACH

INNATE PHARMA VALUE PROPOSITION

CHECKPOINT INHIBITION BEYOND PD-1 PATHWAY BLOCKADE

- Heterogeneity in cancers, between patients or intra tumoral opens opportunity for differentiated novel agents



Patient stratification
and
Combination therapy

- Multiple agents needed to address large population of patients and maximize outcome
  - > IPH compounds target differentiated tumor escape mechanisms
  - > Targeting NK cells expected to be very well tolerated, opening opportunities for multiple combinations

TARGETING NK CELLS

Nature Reviews Drug Discovery | AOP, published online 22 May 2015; doi:10.1038/nrd4506

REVIEWS

CANCER IMMUNOTHERAPY

Therapeutic approaches to enhance natural killer cell cytotoxicity against cancer: the force awakens

Richard W. Childs and Mattias Carlsten

Although natural killer (NK) cells have long been known to have advantages over T cells in terms of their capacity to induce antigen-independent host immune responses against malignancies, their therapeutic potential in the clinic has been largely unexplored.

Checkpoint inhibitors:

Lirilumab | IPH/BMS

Monalizumab | IPH/AZN

Innate Pharma

Anti-CD137 | BMS, **Agonist mAB**

CD16-targeting bispecifics | Affimed

NKp46-targeting bispecifics | Innate

Bispecifics

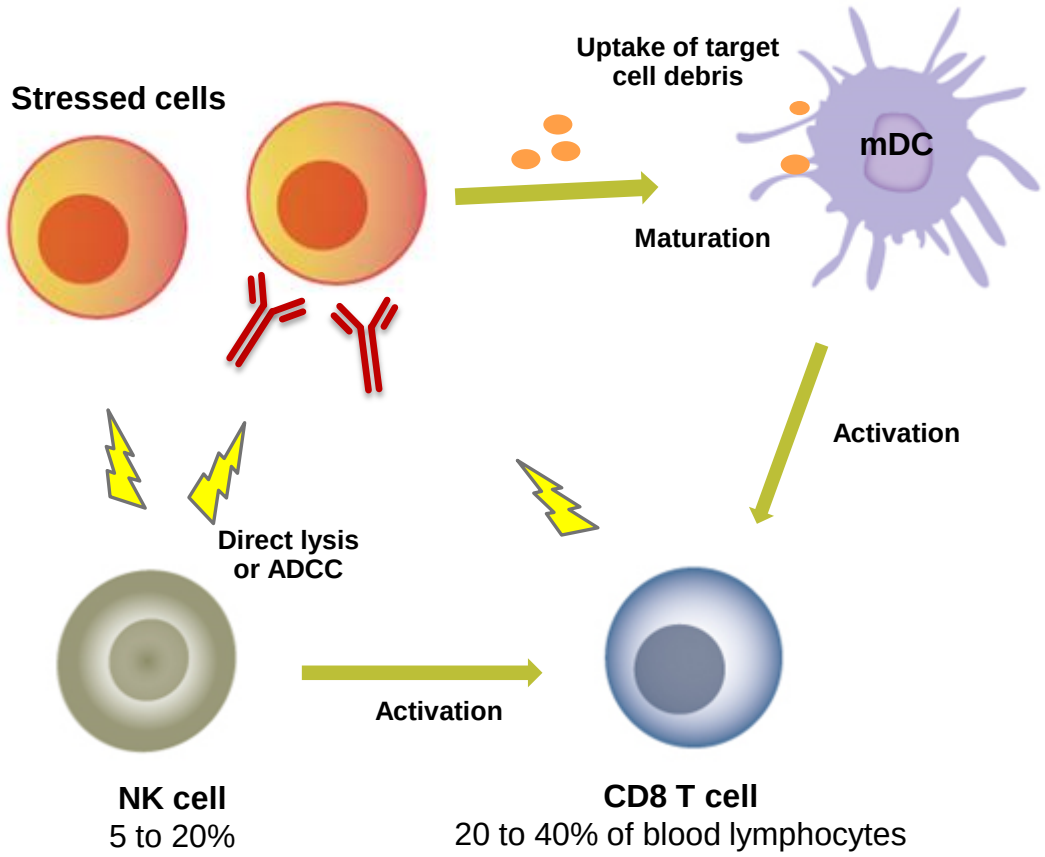
IL-12 - Celsion, **Cytokine**

CEA-IL-2 | Roche,

Antibody-IL2 fusion proteins

CARNK cells | NaNKwest, Celyad, Cytomx, **Cell therapy**

NK CELLS EXERT POTENT ANTI-CANCER FUNCTIONS

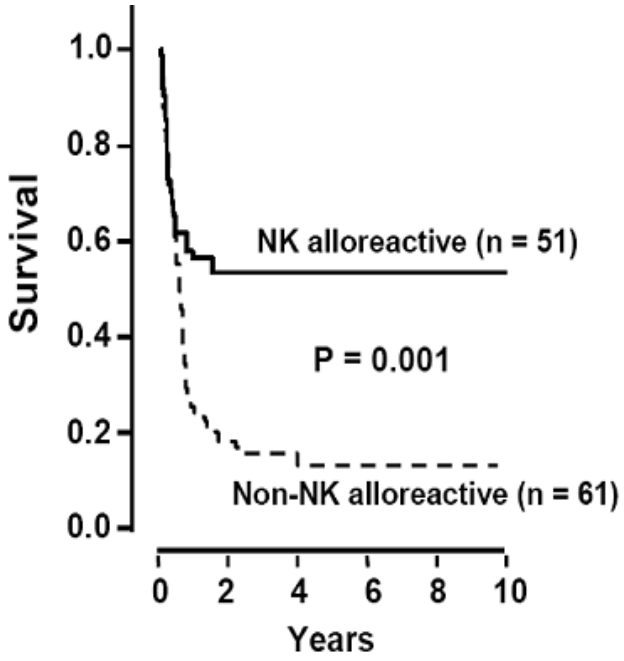


- **Direct cytotoxicity**:
  - > Kill tumors and infected cells
  - > Triggered by conserved stress-antigens
- **Cytokine production:**
  - > e.g. IFN-γ and IL-2 that stimulate T cells
- **Regulatory functions:**
  - > Maturation of antigen presenting cells

Adapted from Vivier et al., Nature Immunology 2008, Vivier et al., Science 2011

THERAPEUTIC POTENTIAL OF NK CELLS
REVEALED IN ACUTE MYELOID LEUKEMIA

- NK cells can protect against tumor relapse, leading to improved survival in AML patients after stem cell transplantation



NK activation

NK inhibition

Effects are:

- Durable
- Safe
- Mediated by NK cells
- Controlled by KIR

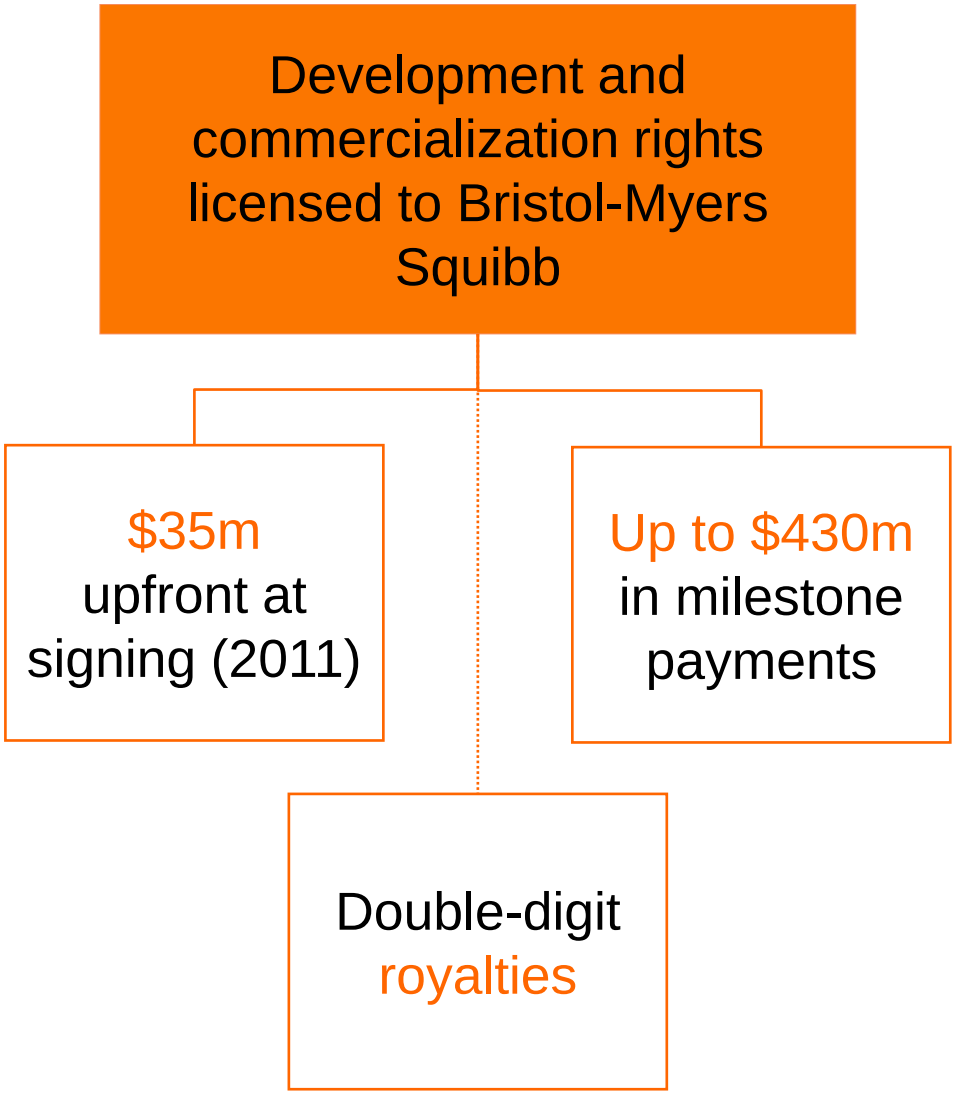
Velardi et al., Science, 2002 (not shown)
Ruggeri et al, Blood, 2007

LIRILUMAB

FIRST-IN-CLASS ANTI-KIR MAB

LICENSED TO BRISTOL-MYERS SQUIBB

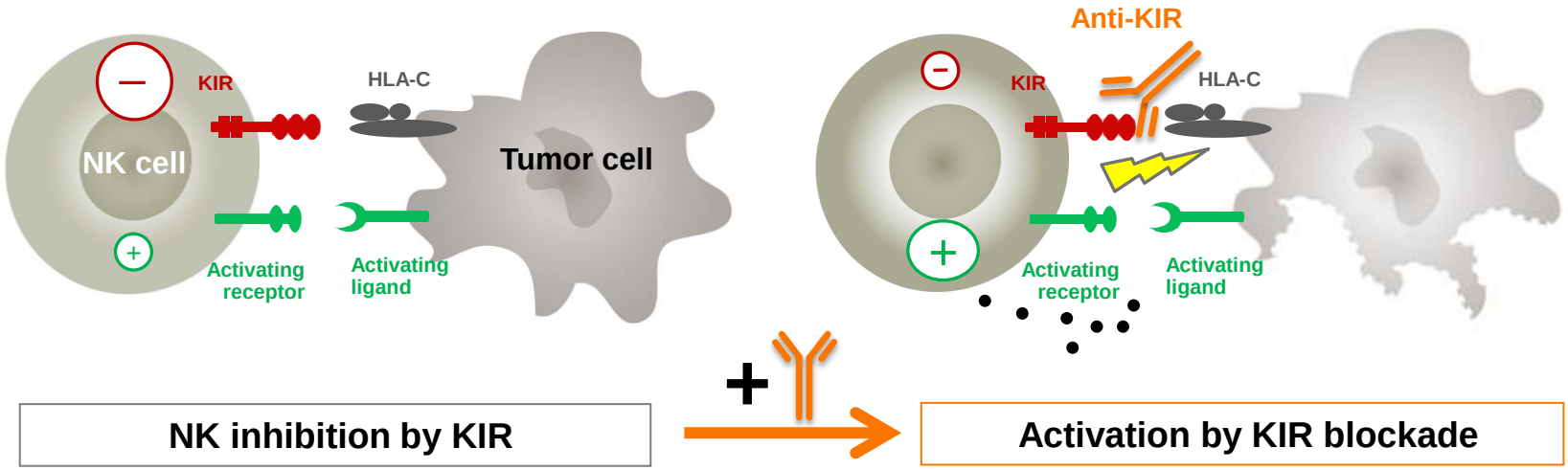
LICENSING AGREEMENT WITH BRISTOL-MYERS SQUIBB



LIRILUMAB

FIRST-IN-CLASS NK CELL CHECKPOINT INHIBITOR

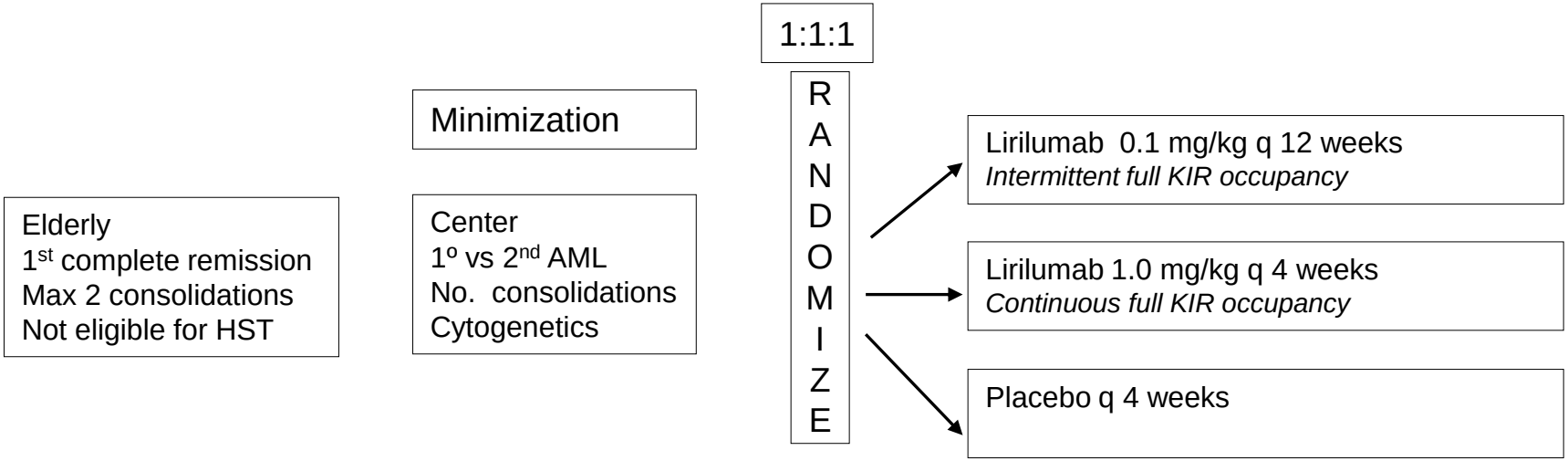
- Fully human antibody (IgG4) blocking NK cell inhibitory receptor KIR2DL1/2/3
- Prevents interaction with HLA class 1 molecules to potentiate NK anti-tumor activity



EFFIKIR PHASE II TRIAL

DOUBLE-BLIND PLACEBO-CONTROLLED RANDOMIZED TRIAL IN AML

- Target enrollment completed in July 2014 (150 patients)
- Data on LFS expected 2H16
- One active arm stopped in March 2015 upon DSMB recommendation
  - > DSMB considered that treatment in the stopped arm could not be superior to placebo. There was no concern with tolerance



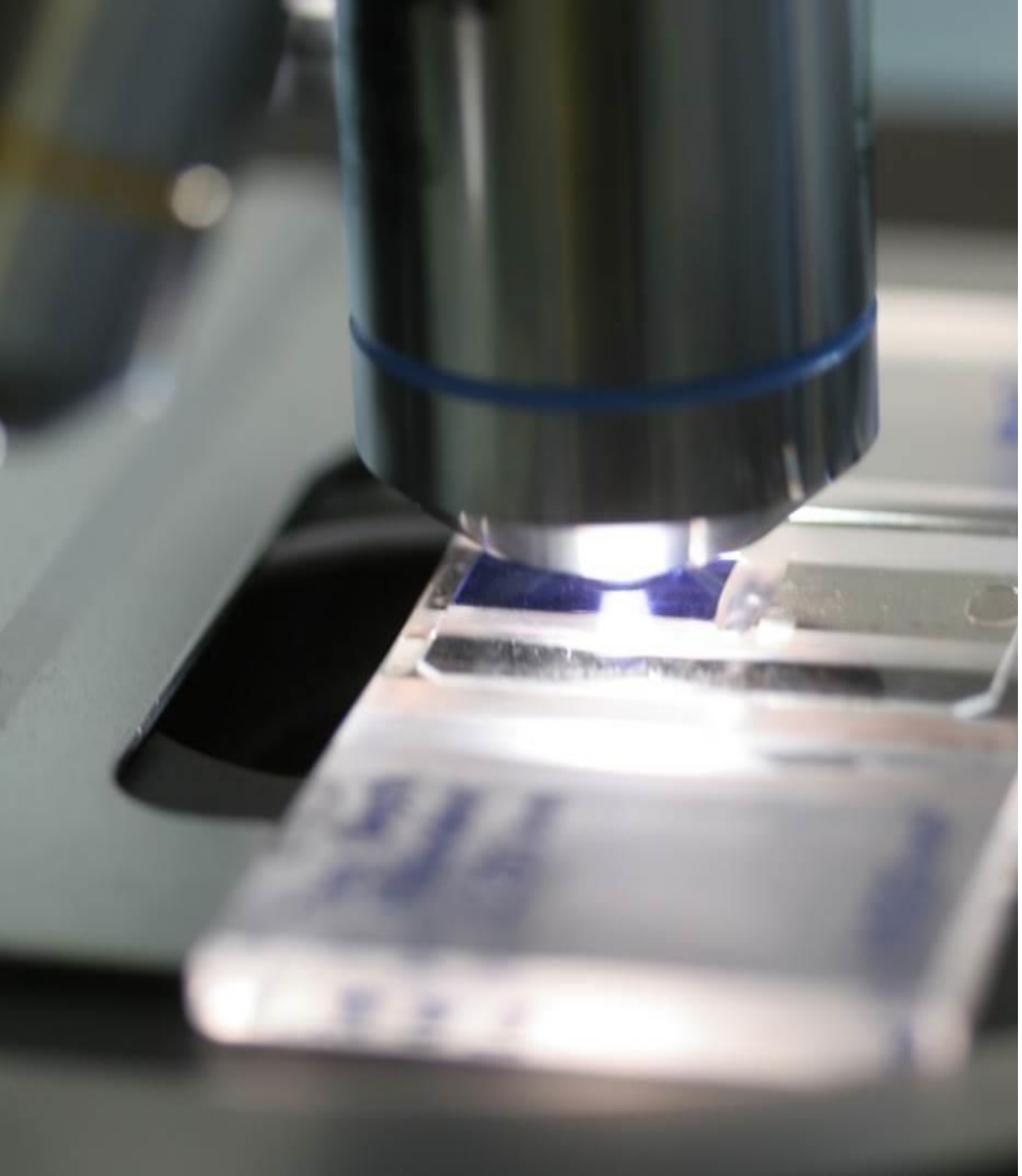
Treatment for 2 years
Primary endpoint: Leukemia-Free Survival (Independent Review Committee)
N=50 per arm
Maximum follow-up period: 24 months after last patient entry

ClinicalTrials.gov Identifier: **NCT01687387**

CLINICAL PROGRAM WITH LIRILUMAB

		SETTING	PATIENTS	INDICATION	STATUS
	Monotherapy	Randomized Phase II	150	Acute Myeloid Leukemia Maintenance setting	Data on LFS expected 2H 2016
Combination	Nivolumab	Phase I with cohort expansion	162	Selected solid tumors: MEL, NSCLC, GI, SCCHN, HCC	Enrollment close to completion
	Nivolumab	Phase I	315(1)	Selected hematologic tumors: R/R NHL, HL, MM or CML	Started October 2014
	Elotuzumab	Phase I with randomized cohort expansion	136(2)	Multiple Myeloma: R/R MM Post autologous transplant	Started October 2014
	Rituximab	Phase II	48	Chronic Lymphocytic Leukemia R/R or High-risk Untreated	Started June 2015
	5-azacytidine (Vidaza)	Phase II with dose escalation	64	Acute Myeloid Leukemia Relapsed/refractory	Started April 2015
	Nivolumab 5-azacytidine	Phase II	80	Myelodysplastic Syndromes (MDS)	Started November 2015

R/R: relapsed / refractory (1) Three arms (nivo, nivo + ipi, nivo + liri) / (2) Two arms (elo + liri, elo + ure)



MONALIZUMAB

FIRST-IN-CLASS ANTI-NKG2A MAB

CO-DEVELOPMENT AND COMMERCIALIZATION AGREEMENT WITH ASTRAZENECA

CO-DEVELOPMENT AND COMMERCIALIZATION AGREEMENT WITH ASTRAZENECA

Global co-development and commercialization agreement for monalizumab

$250m initial payment (June 2015)

$100m prior to initiation of Phase III

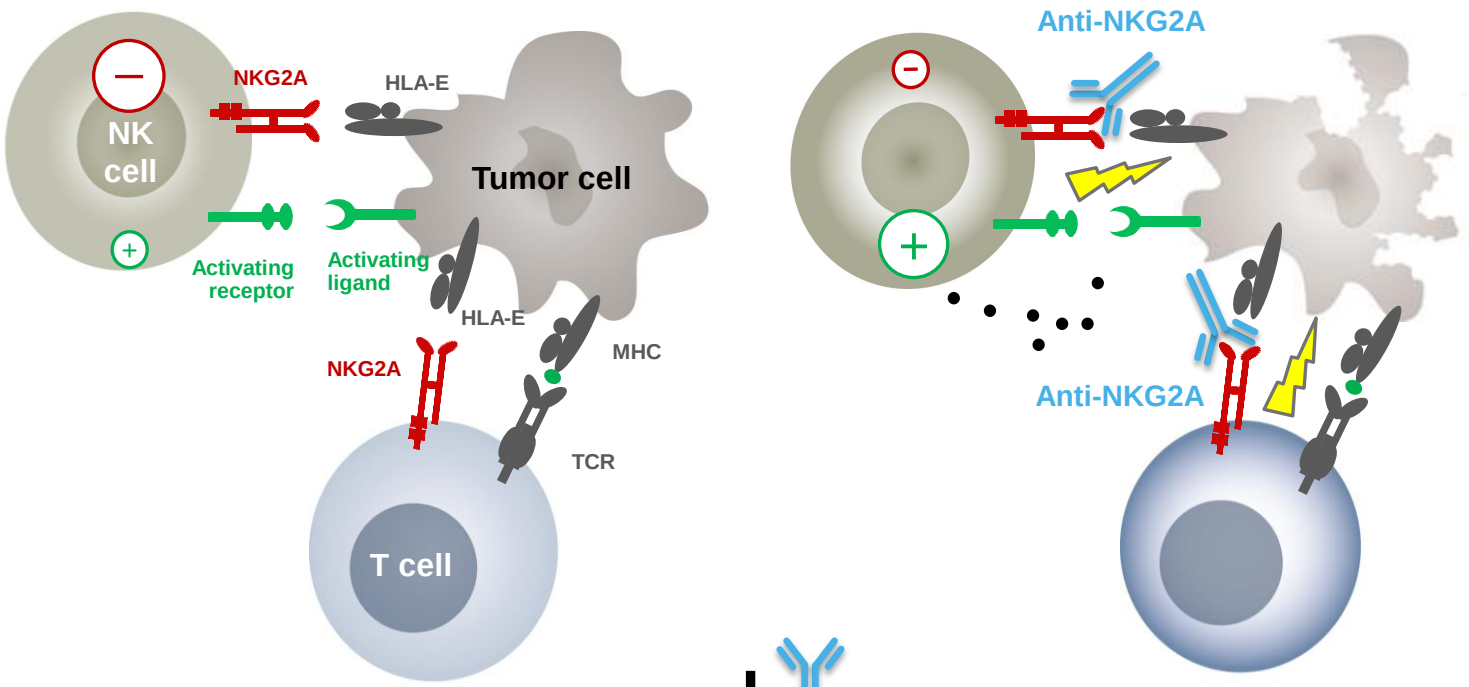
up to $925m additional milestones

Co-promotion rights in Europe (50% profit)

Double-digit royalties

MONALIZUMAB (IPH2201) TARGETS NKG2A CHECKPOINT ON NK AND CD8 T CELLS

- NKG2A is an inhibitory receptor on tumor infiltrating CD8 T cells and NK cells



NK and T cell inhibition by NKG2A

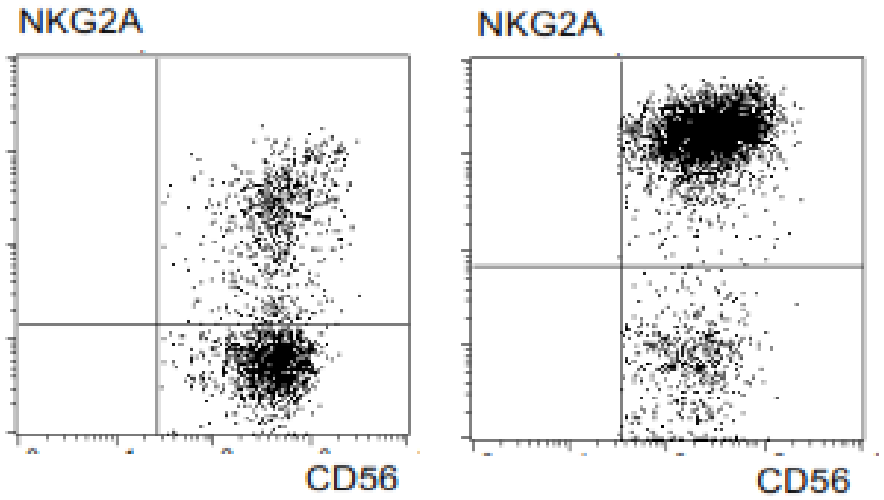
Activation by NKG2A blockade

NKG2A IS EXPRESSED ON TUMOR INFILTRATING LYMPHOCYTES

Upregulation of NKG2A
on NK cells inside tumors

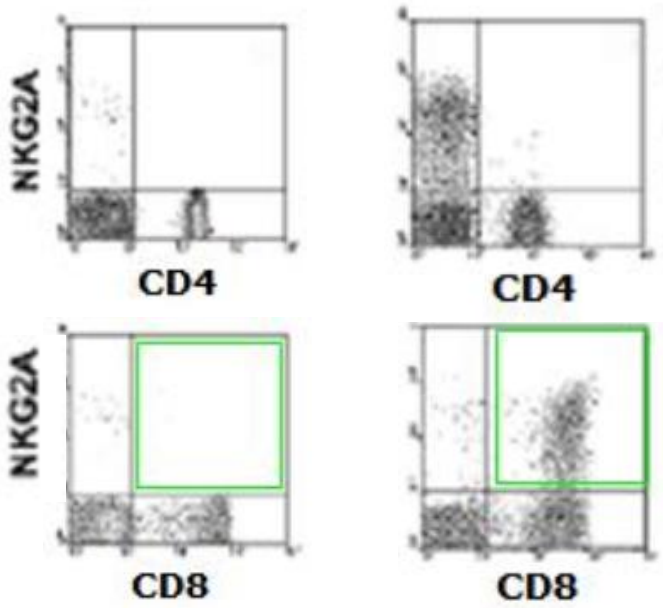
NKG2A on tumor infiltrating
$CD8^+$ T cells

Lung carcinoma



Blood NK (HC) **Intratumoral NK**

Cervical cancer

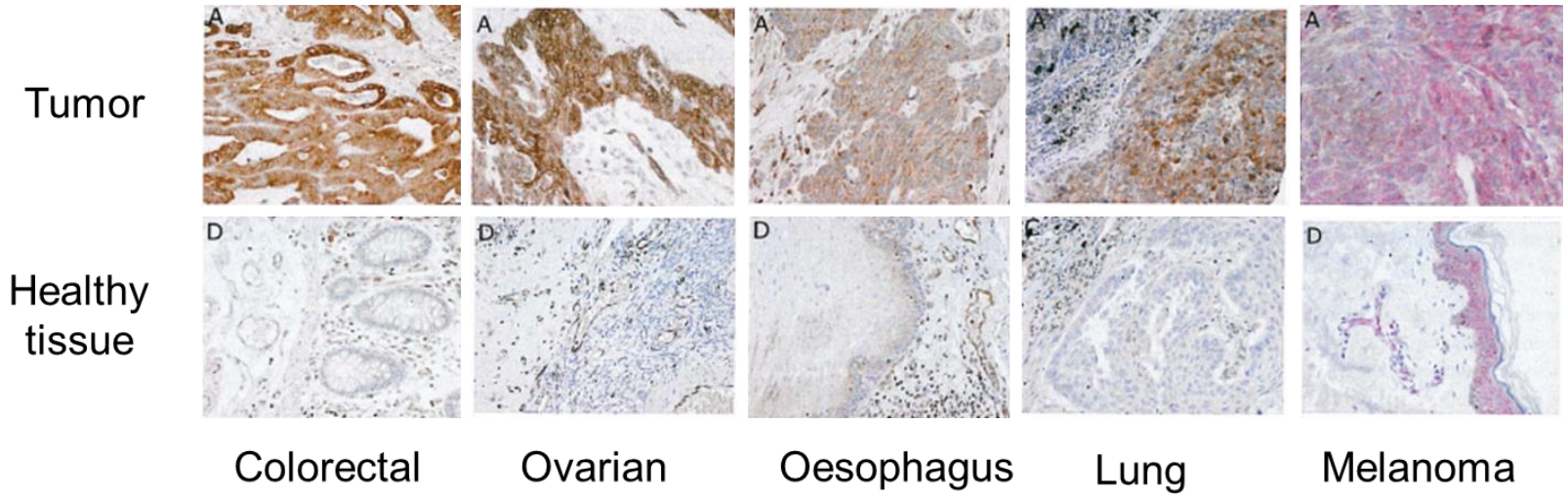


Blood T cell **Intratumoral T cell**

From L to R : Platonova et al. 2011, Sheu et al. 2005

CLINICAL DEVELOPMENT PLAN INFORMED BY EXPRESSION OF HLA-E

- Many tumors overexpress HLA-E, the ligand of NKG2A, suggesting a major mechanism of immune evasion
- HLA-E upregulated on a wide variety of tumor types
  - > Ovarian (>70%)[1], Head and Neck (~80%)[2], Colorectal (>80%), Lung (40%), CLL (>90%)[3], Oesophagus etc
- Restricted expression on normal tissues



Source: 1. **Gooden, OncoImmunol, 2012;** ***2. Levy, Sycz et al. 2009; Nasman, Andersson et al. 2013, 3.*** **Veuillen, Aurran-Schleinitz et al. 2012**

MONALIZUMAB

INITIAL CLINICAL DEVELOPMENT PLAN TO GENERATE DATA IN 2017

		SETTING	PATIENTS	INDICATION	STATUS	LOCALIZATION
	Monotherapy	Phase I/II	43	Head & Neck Neo-adjuvant setting	Started Dec. 2014	Europe
	Monotherapy	Phase I/II	38	Ovarian cancer High grade platinum sensitive or resistant	Started Sept. 2015	Canada
Combination	Ibrutinib	Phase I/II	Up to 45	Chronic Lymphocytic Leukemia Relapsed or refractory	Started Oct. 2015	US
Combination	Cetuximab	Phase I/II	Up to 70	Head & Neck Relapsed or refractory	Started Dec. 2015	US and Europe
Combination	Durvalumab (anti-PD-L1)	Phase I with cohort expansion	Up to 208	Solid tumors	Started Feb. 2016	US and Europe

IPH4102

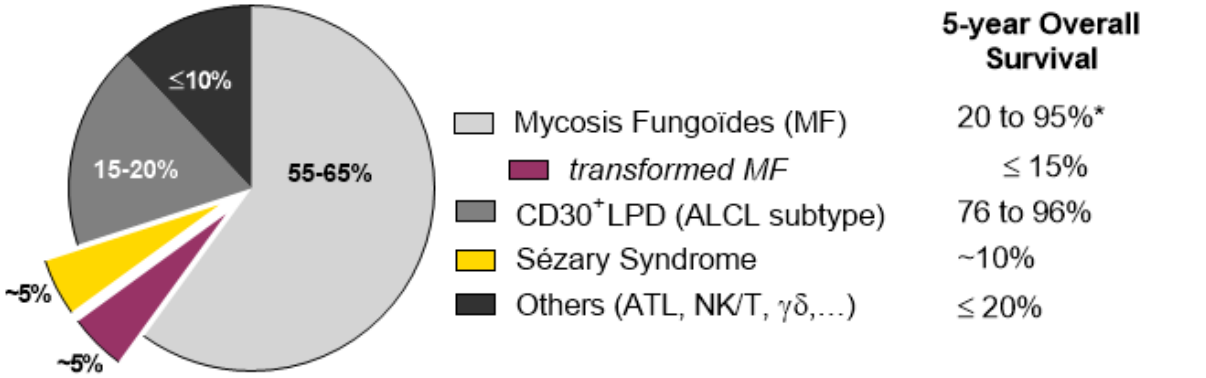
FIRST-IN-CLASS ANTI-KIR3DL2 CYTOTOXIC MAB

IN-HOUSE DEVELOPMENT

CUTANEOUS T CELL LYMPHOMA

ORPHAN DISEASE WITH HIGH MEDICAL NEED

- CTCL is a heterogeneous group of T-cell NHL presenting primarily in the skin
  - > ~6,000 patients in EU and US
  - > Mycosis fungoides (MF) and Sézary syndrome (SS), its leukemic variant, are the most common CTCL subtypes
  - > Overall survival depends in part on disease subtype



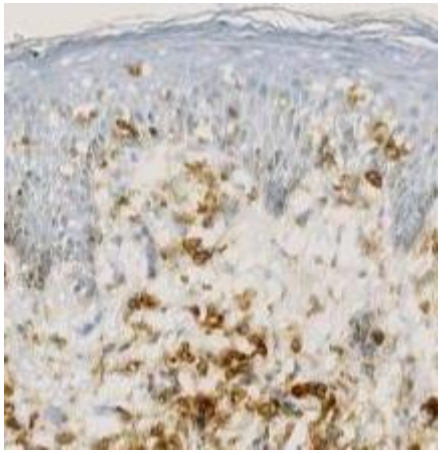
- No standard of care in CTCL. Need for more options, inducing durable responses, particularly in SS and transformed MF.

KIR3DL2 IS SPECIFICALLY EXPRESSED ON CUTANEOUS AND CIRCULATING CTCL CELLS

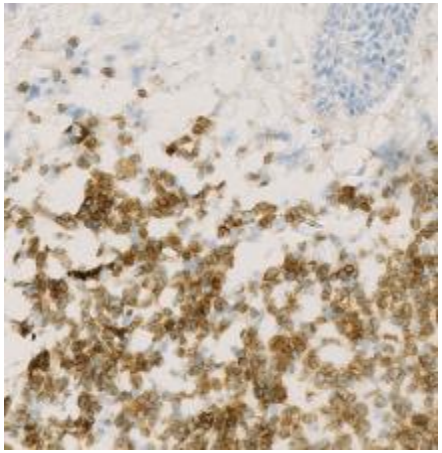
- Irrespectively of disease grade and on most subtypes
  - > ~65% of all CTCL;
  - > Expression is more prominent in Sézary syndrome, transformed mycosis fungoides and CD30+ LPD (ALCL subtype): from 80% to 100% of patients
- Restricted expression on normal tissues

Patients biopsies stained with Innate's anti-KIR3DL2 mAb

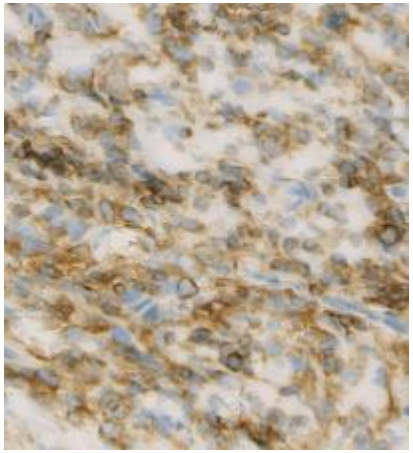
SS pt #1, grade IIIB
86.5% KIR3DL2$^+$ tumor cells



tMF pt #1, grade IIB
96% KIR3DL2$^+$ tumor cells



CD30$^+$ LPD pt #3, grade IB
81% KIR3DL2$^+$ tumor cells

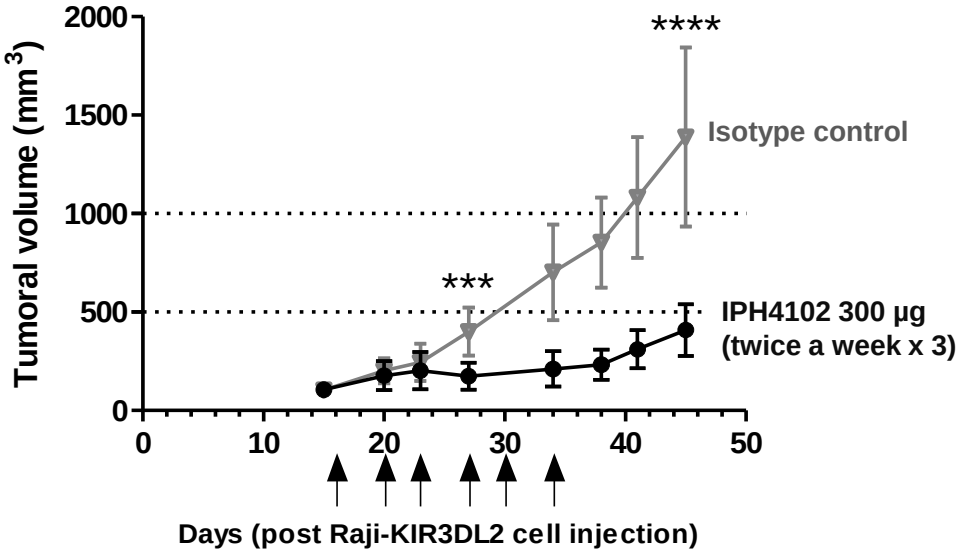


CTCL: cutaneous T cell lymphoma

POTENT ANTITUMOR ACTIVITY OF IPH4102 IN MODELS OF ADVANCED CTCL

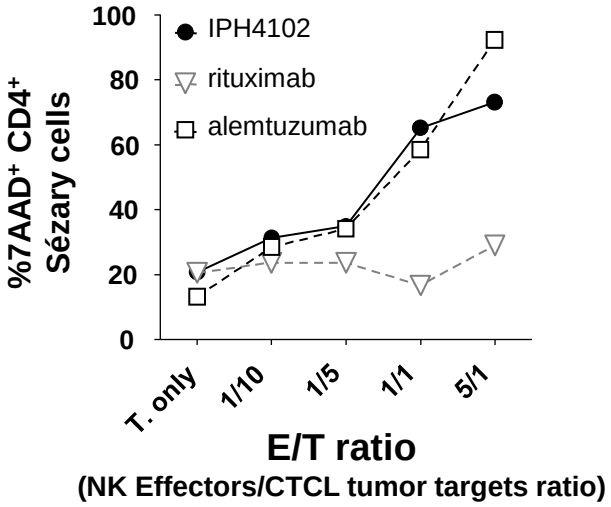
- Humanized cytotoxic IgG1

RAJI-KIR3DL2 SC xenograft model



Autologous ADCC with CTCL patient cells

Patient #10 (representative of n = 15)



http://innate-pharma.com/sites/default/files/150926_eortc_bagot_neil_smith_2.pdf
http://innate-pharma.com/sites/default/files/20151002_iph4102-101_study.pdf
Collaboration with St Louis Hospital, Paris

PHASE I STUDY OF IPH4102 STARTED IN 2015

- Dose-escalation + cohort expansion study:
  - > Dose-escalation: 10 dose levels of repeated administrations of IPH4102
  - > Cohort expansion: 2 cohorts of 10 patients each in SS and tMF
    - Displaying most robust KIR3DL2 expression
    - Highest unmet medical need
- EU and US, involving referral expert centers:
  - > St Louis Hospital, Paris (Pr M. Bagot)
  - > UMC Leiden, the Netherlands (Dr M. Vermeer)
  - > Guy's and St Thomas' Hospital, London UK (Pr S. Whittaker)
  - > Stanford U., CA, US (Pr Y. Kim)
  - > MD Anderson, Houston, TX, US (Pr M. Duvic)
  - > OSU, Columbus, OH, US (Pr P. Porcu)

- Completion of dose escalation expected in 2017 and completion of cohort expansion expected in 2018
- Orphan drug status in EU for the treatment of cutaneous T-cell lymphoma
- For further information, see on our website in the IPH4102 section:
  - > Talks by Pr. Kim – New York, October 2015 / Pr. Bagot – Paris, December 2015

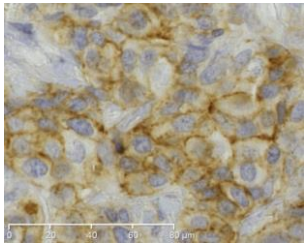
DISCOVERY

IPH43 (ANTI-MICA/B)

ANTI-CD39

IPH43
FIRST-IN-CLASS ANTI-MICA/B MAB

- MICA/B is a ligand for the activating receptor NKG2D expressed on NK cells and CD8+ T cells. Its expression is induced upon tumoral transformation

A.


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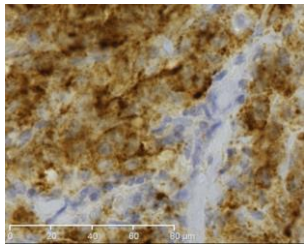

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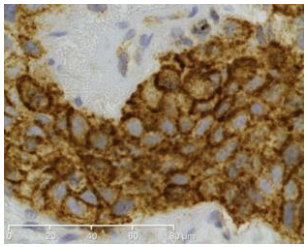

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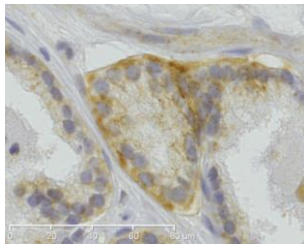


Tissue	Positive/Total cases	% Positive
A. Breast Cancer	24/29	83%
B. Colo-rectal Cancer	17/28	61%
C. Lung Cancer	18/28	64%
D. Prostate Gland	3/5	-

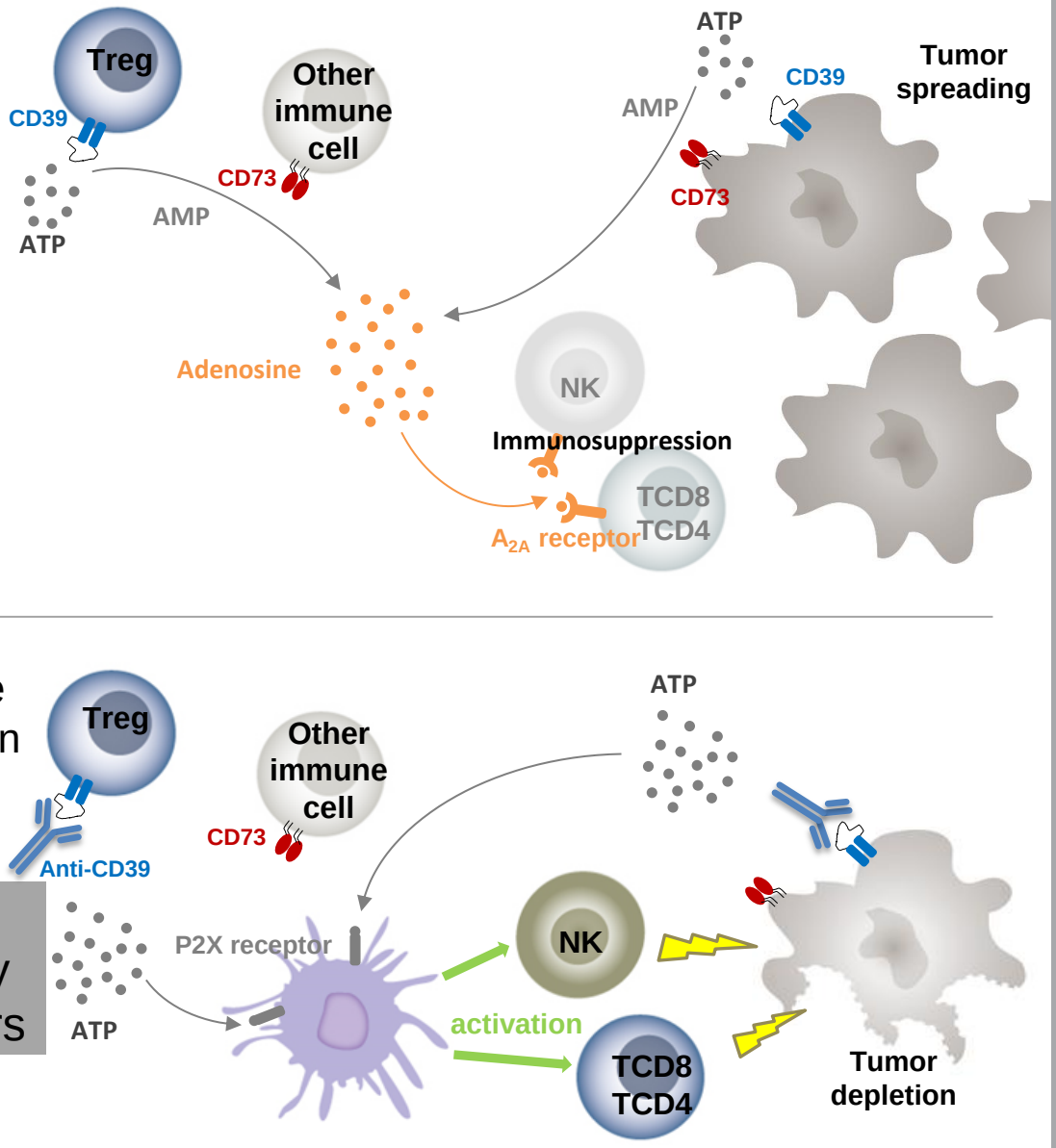
- However, chronic exposure to MICA/B downregulates NKG2D
- MICA/B is also expressed on tumor associated immunosuppressive macrophages

IPH43 could display a dual mechanism of action: tumoral antigen targeting and immunomodulation

DISCOVERY:

FIRST-IN-CLASS ANTI-CD39 CHECKPOINT INHIBITOR PROGRAM

- CD39 is expressed on both regulatory T cells and tumor cells
  - > CD39 promotes the immunosuppression through the pathway degrading ATP into adenosine
  - > ATP promotes immune cell-mediated killing of cancer cells. In contrast, adenosine accumulation causes immune suppression and dysregulation of immune cell infiltrates resulting in tumor spreading
- Blockade of CD39 may stimulate anti-tumor immunity across a wide range of tumors



ATP : adenosine triphosphate

KEY CORPORATE AND FINANCIAL FACTS

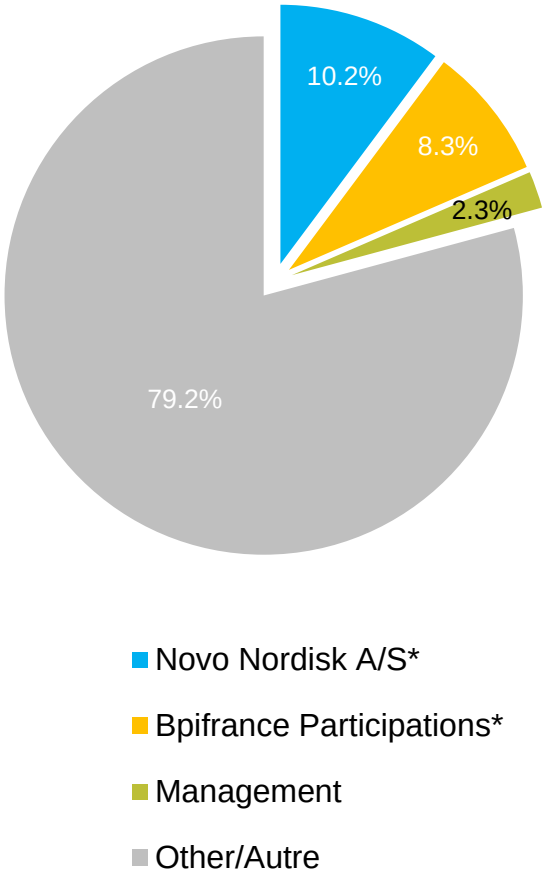
KEY FIGURES

In thousand euros (IFRS)	Year ended December 31 2015	2014
Revenue and other income	**25,141**	**7,623**
Research and development expenses	(29,906)	(22,671)
General and administrative expenses	(6,008)	(4,918)
Net operating expenses	**(35,914)**	**(27,589)**
Operating income / (loss)	**(10,772)**	**(19,966)**
Financial income / (expense), net	4,066	508
Net income / (loss)	**(6,706)**	**(19,647)**
Weighted average number of shares (in thousands):	53,400	50,152
Net income (loss) per share	(0.13)	(0.39)

	2015	2014
Cash, cash equivalents and financial instruments	**273,704**	**69,238**
Total financial liabilities	3,754	4,206

SHARE INFORMATION

- Listed on Euronext, IPO in November 2006
  - > Euronext Paris: FR0010331421 – IPH
  - > Unsponsored ADR: INNTY
- Stock liquidity (in 2015)
  - > Average daily trading volume >300,000
  - > 53.8m outstanding shares (55.7 fully diluted)
- Analyst coverage:
  - > Bryan Garnier
  - > Citi
  - > Gilbert Dupont
  - > Goldman Sachs
  - > Invest Securities
  - > Leerink Partners
  - > Oddo Securities
  - > Portzamparc



* Shareholders represented at the Supervisory Board

MANAGEMENT TEAM

Hervé BRAILLY
PhD,
CEO & Co-founder

Immunotech SA, Beckman-Coulter

Catherine MOUKHEIBIR
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Sr Advisor Finance

Movetis, Zeltia, Morgan Stanley

Jérôme TIOLLIER
PhD,
Chief Development Officer
Pasteur Merieux Sangstat

Nicolai WAGTMANN
PhD,
Chief Scientific Officer
Novo Nordisk A/S

Pierre DODION
MD, MBA,
Chief Medical Officer
ARIAD, Pfizer, Novartis, Aventis

Yannis MOREL
PhD,
Chief Business Officer
Innate Pharma

Marcel ROZENCWEIG
MD,
President, Innate Pharma Inc.

BMS

UPCOMING Q1 IR EVENTS

Conference call for annual results
Paris, France - February 18, 2016

Credit Suisse
Global Healthcare Conference
London, UK - March 1, 2016 to March 2, 2016

BAML / Group Investor Bus Trip
Paris, France - March 8, 2016

Oddo Biotech/Medtech Forum
Paris, France - March 31, 2016

Portzamparc Event PEA PME
Paris, France - April 5, 2016

Kempen & Co Healthcare
Life Sciences Conference
Amsterdam, Netherlands - April 7, 2016

SmallCap Event
Paris, France - April 11 & 12, 2016

AACR Annual Meeting 2016
New Orleans, USA - April 16, 2016 to April 20, 2016

INVESTOR RELATIONS

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APPENDIX

LIRILUMAB
APPENDIX

PHASE I WITH LIRILUMAB

- Single-agent Phase I with a variety of hematologic and solid tumors
  - > Slowly progressive or stable disease or in complete response
  - > Does not allow assessment of tumoral response
- Primary endpoint: safety; secondary endpoints: PK/PD
- 37 patients treated, at 6 dose levels from 0.015 mg/kg to 10 mg/kg
- Well tolerated, no dose limiting toxicity, maximum tolerated dose not reached
  - > Most frequent related TEAEs included: fatigue/asthenia, pruritus, infusion related reaction, headache
  - > Low incidence of grade 3-4, treatment related AEs
  - > Reported across all dose levels, no clear dose relationship

Patients with treatment-emergent AEs							
Type of AEs	**0.015 mg/kg (n=12)**	**0.3 mg/kg (n=3)**	**1 mg/kg (n=4)**	**3 mg/kg (n=12)**	**6 mg/kg (n=3)**	**10 mg/kg (n=3)**	**Total (n=37)**
Any grade 3/4*	7 (58%)	2 (67%)	3 (75%)	9 (75%)	2 (67%)	2 (67%)	25 (68%)
Related grade 3/4	4 (33%)	0	0	2 (17%)	1 (33%)	0	**7 (19%)**
Any AE leading to study drug discontinuation	3 (25%)	0	1(25%)	1(8%)	0	2(67)	7 (19%)
Related AE leading to study drug discontinuation	3 (25%)	0	0	0	0	0	**3 (8%)**

* 7 (18.9%) = Disease progression

Source: Vey et al., ASCO 2015 poster

CLINICAL EXPERIENCE WITH HYBRIDOMA ANTI-KIR IPH2101

PHASE I IN ACUTE MYELOID LEUKEMIA

- Elderly AML patients in complete remission after induction and consolidation treatment - maintenance setting
- Phase I dose-escalation including 23 patients in first CR, and extension including 12 patients
- Doses ranged from 0.0003 to 3 mg/kg – Full KIR saturation at doses ≥1mg/kg
- Good tolerance with mild and transient adverse events. MTD not reached. Clear PK/PD relationship
- Clinical outcome (2 patients from extension excluded, one in CR2 and one for early relapse within 5-days)

Dose	N*	PFS (months)	OS (months)
<1 mg/kg	16	2. 3	12.6
1-3 mg/kg	16	9.5	20.0
HR (95%CI)		0.515 (0.245; 1.081)	0.490 (0.219; 1.096)
P-value		0.075	0.076

Sources: Vey et al., Blood Sept. 21 and ASH 2013 poster

CLINICAL EXPERIENCE WITH HYBRIDOMA ANTI-KIR IPH2101
COMBINATION PHASE I IN MULTIPLE MYELOMA

- Phase I dose-escalation of IPH2101 in combination with lenalidomide (LEN) in 15 patients with relapsed/refractory MM
  - > Prior therapies: one prior line: 10 pts; 2 prior lines: 5 pts; prior LEN: 10 pts
- Treatment
  - > 4 cycles of IPH2101 and LEN; 5 pts received 4 additional cycles
  - > No use of corticosteroids
- Results
  - > Combination generally well tolerated
  - > IPH2101 PK and PD not affected by co-administration of LEN
  - > Objective responses observed in 33.3% of patients with and without prior LEN exposure. Median PFS of 24 months

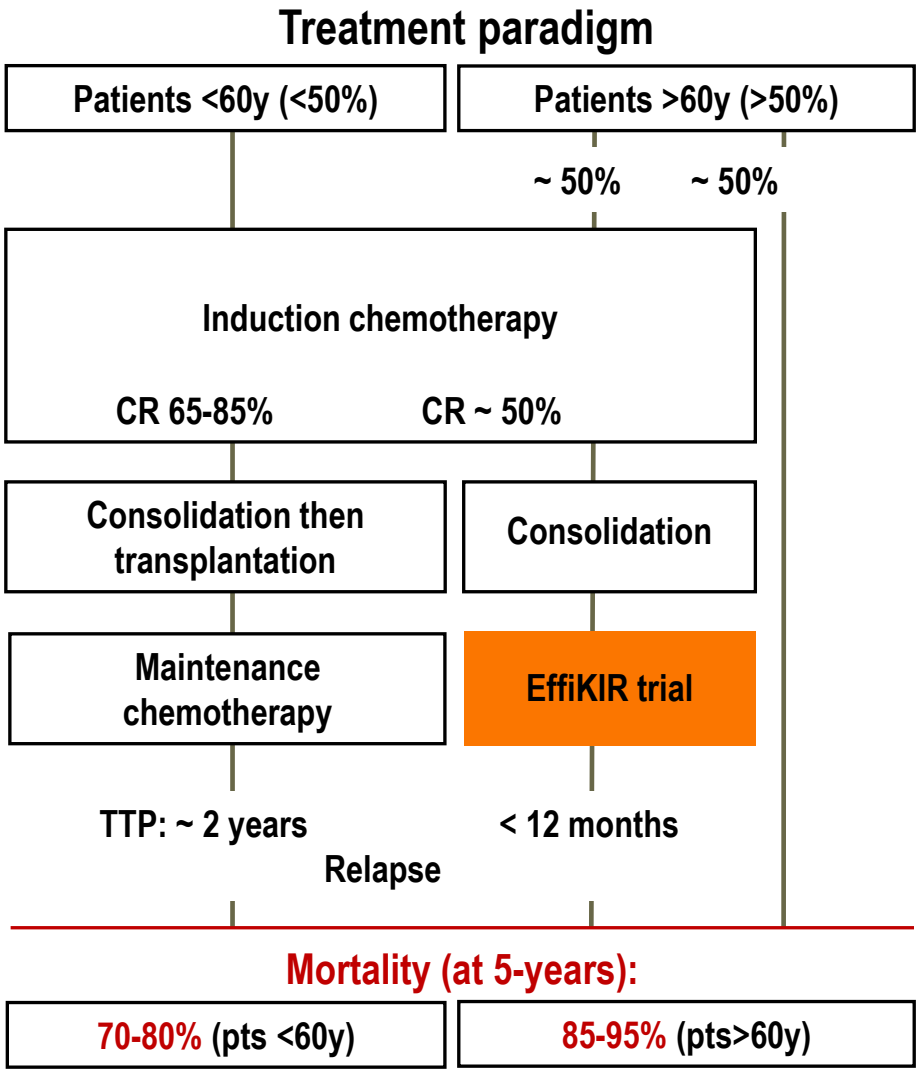
Overall best response	Total	Dose lirilumab - LEN		
		0.2mg/kg - 10mg	0.2 mg/kg - 25mg	1 mg/kg - 25mg
VGPR	2 (13.3%)	1	0	1
PR	3 (20%)	1	1	1
MR/SD	7 (46.7%)	3	0	2

***Source: Benson et al., ASH 2013 poster, Clinical Cancer Research*, 2015**

EFFIKIR POSITIONING IN ACUTE MYELOID LEUKEMIA

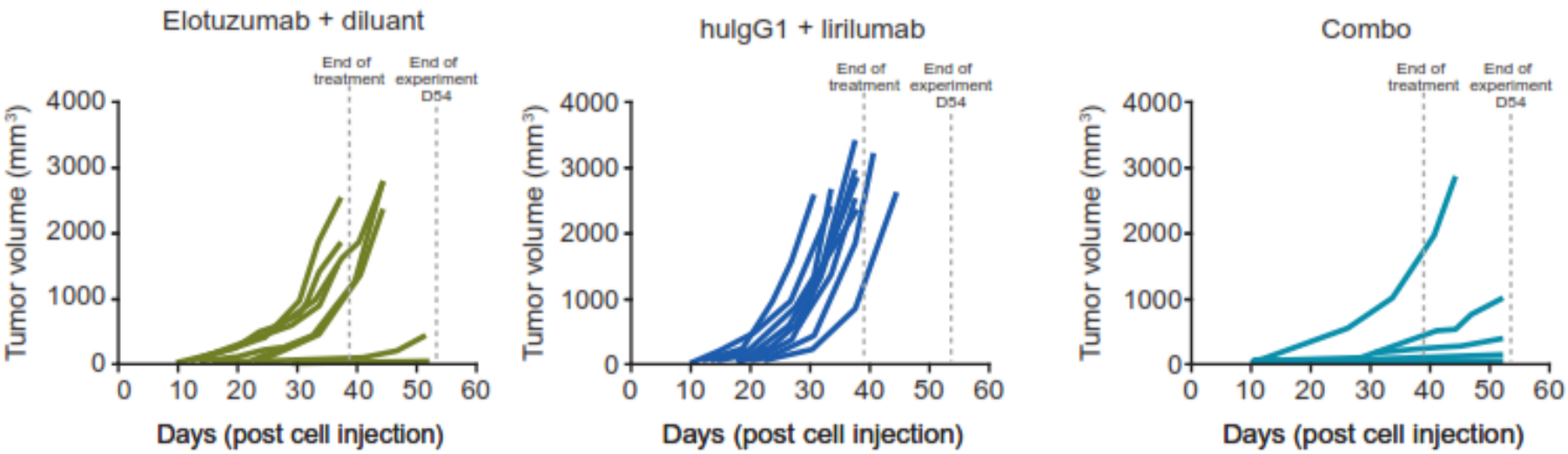
STRONG MEDICAL NEED IN ELDERLY PATIENTS

- 5-year survival rate in elderly patients with AML is 5 to 15%
- No current standard of care for elderly patients in post-induction setting
- Intensive development effort in AML focused on relapsed / refractory disease
- Lirilumab tested in maintenance for elderly patients



LIRILUMAB ENHANCES ADCC FUNCTION OF NK CELLS

***In vivo* effects of KIR blockade (lirilumab) on elotuzumab activity in xenograft tumor model**



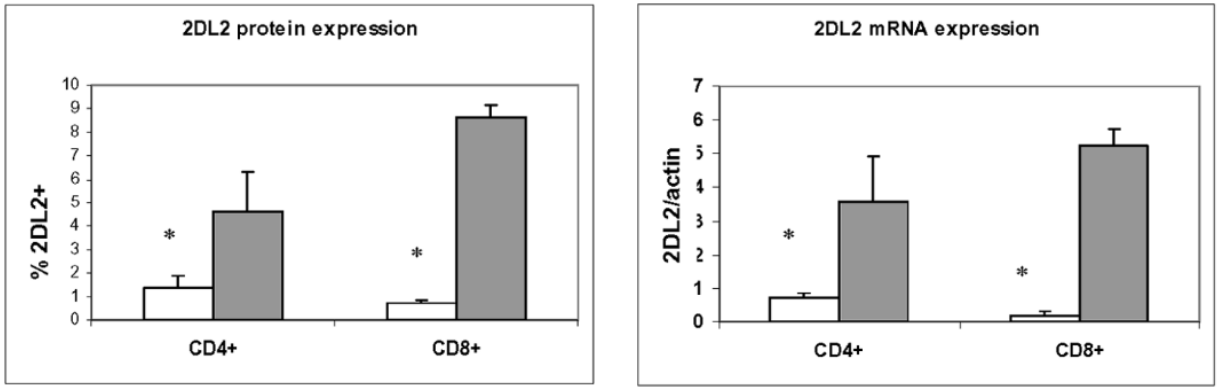
Mice with established OPM-2 xenograft tumors (n=10, per treatment group) were treated with elotuzumab (0.5 mg/kg, biweekly from Day 11) , IgG1 plus liriumab (IPH2102, 15 mg/kg, Days 11 and 24), or elotuzumab plus liriumab. Data represent tumor volume for individual animals that had tumor growth.

Robbins et al., Poster ASH 2014

LIRILUMAB IN COMBINATION WITH HYPOMETHYLATING AGENTS

- Hypomethylating agents are epigenetic modifiers
- 2 of these drugs have been approved:
  - > 5 azacytidine in high risk myelodysplastic syndrome (MDS) (US and EU)
  - > decitabine as palliative treatment of acute myeloid leukemia (US only)
- These agents upregulate the transcription of NKG2D ligands, MICA/B and ULBP, which trigger the activation of NK cells (Chretien, 2014; Krieg, 2013).
- They also upregulate KIR2D expression limiting thus the enhancement of NK and T cell anti tumor functions (Liu, 2009)

Effect of 5-azaC on T cell KIR2DL2 expression



Costello et al, 2015; Gang et al, 2014; Liu et al, 2009; Rohner et al, 2007

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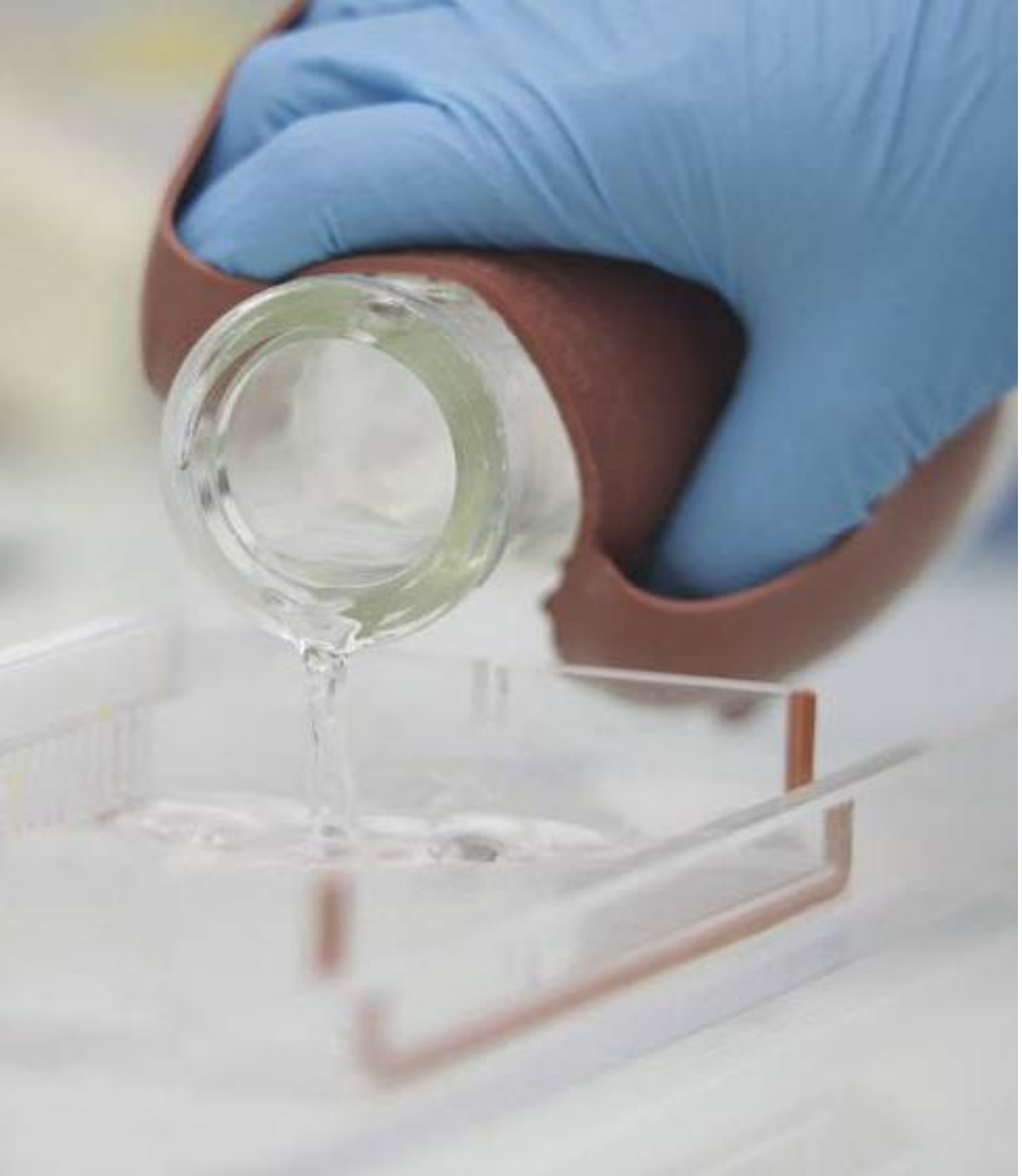
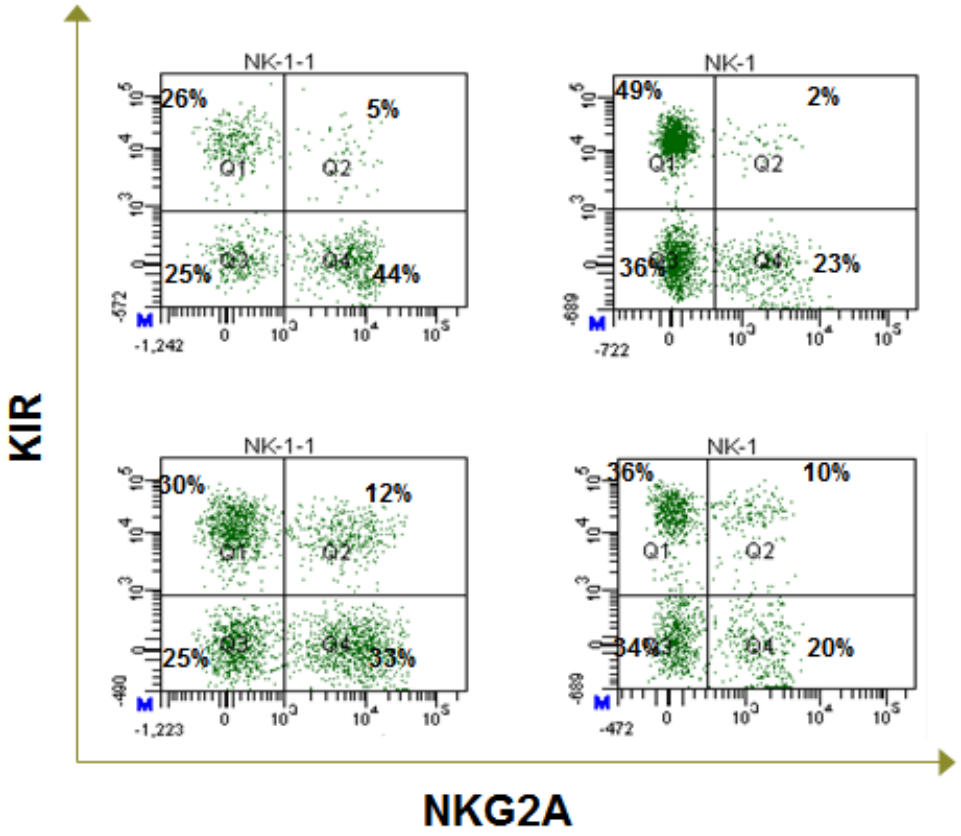


MONALIZUMAB
APPENDIX

KIR AND NKG2A EXPRESSION
ON DIFFERENT SUBSETS OF NK CELLS

- Blood NK cells from four healthy donors (one in each panel) stained for KIR and NKG2A



Internal data

MONALIZUMAB
PHASE I SAFETY DATA

- Good safety profile in Phase I

→ Dose-escalation safety trial in rheumatoid arthritis patients

- 92 pts, mild to moderate severity RA, low-dose MTX
- IV single dose (up to 10 mg/kg) and SC single and multiple doses (up to 4 mg/kg)
- No safety issues identified, MTD not reached, no DLT

- Dose-escalation safety trial completed in 2014 – publication in preparation

SQUAMOUS CELL CARCINOMA OF THE HEAD AND NECK (SCCHN)
TREATMENT STRATEGY IN LOCALLY ADVANCED DISEASE

- SCCHN is the sixth most common cancer worldwide[1] (estimate)
  - > 650,000 cases and 200,000 deaths /yr worldwide, most common cancer in Asia[1]
  - > At diagnosis, 60% patients have locally advanced disease; when metastatic at presentation or recurrent and/or metastatic after initial treatment, usually incurable
- SOC in locally advanced disease:
  - > Surgery and cisplatin-based chemo-radiation[2]
  - > The majority of these patients develop local and/or regional recurrences
  - > Distant metastases in 20-30% pts[3]
  - > 1-y survival after surgery ± 80%; 5-y DFS and OS of operated patients ≤ 50-60%[4,5]
- SOC in recurrent and/or metastatic SCCHN:
  - > Cetuximab only targeted agent approved in US and EU
  - > As a single agent in this population, yields only modest activity (9% to 13% response rate, median time to progression of 70 to 105 days)[8,9]

- HLA-E is expressed in about 80% of patients with SCCHN and associated with histopath grade of laryngeal tumors[7]
- SCCHN tumor infiltrating lymphocytes express NKG2A[6]
- NK activation by SCCHN cells is enhanced by monalizumab[7]
- Monalizumab expected to enhance ADCC of cetuximab

1.Globocan Project Geneva: WHO, 2010; 2.ESMO Guidelines; Gregoire V, Ann Oncol 2010; 3. Marur S, Mayo Clin Proc 2008; 4. Licitra, Grandi et al. 2003; 5. Zhong, Zhang et al. 2013, 6.Katou F, Cancer Res 2007; 7. Levy, Sycz et al. 2009; Nasman, Andersson et al. 2013; 8. Vermorken, Trigo et al. 2007; 9. Seiwert, Fayette et al. 2014

OVARIAN CANCER

TREATMENT STRATEGY IN HIGH GRADE PRETREATED PATIENTS

- 5th most common site of all cancers in women, leading cause of death in gynecologic cancers
  - > Overall incidence : 12/100,000 (21,290 estimated new cases in US in 2015)
- Most common subtype is high grade serous carcinoma (~60% of all cases)
- Standard of care:
  - > Newly diagnosed cases: extensive surgery and multiagent chemotherapy
  - > In case of early relapse (“platinum resistant”): salvage chemotherapy
  - > In case of late relapse (“platinum sensitive”): retrial of platinum-based chemotherapy
- Cure remains elusive for the majority of patients with stage III and IV disease
  - > Overall 5-year survival rate is around 30%

- HLA-E is upregulated in 70 to 80% of patients with ovarian cancer; HLA-E overexpression is a poor prognostic factor in gynecologic tumors.
- Presence of tumor-infiltrating lymphocytes correlates with improved outcome especially in those cancers with high HLA-E expression

***Gooden, OncoImmunol, 2012*; Zhang, N Engl J Med, 2003; Sato, PNAS, 2005**

CHRONIC LYMPHOCYTIC LEUKEMIA

TREATMENT STRATEGY IN RELAPSED OR REFRACTORY DISEASE

- Most common form of leukemia, accounting for about 25% of all leukemias
  - > Overall incidence : 15,720 new cases will occur in 2014 in the US, causing 4,600 deaths (Siegel, Ma et al., 2014)
  - > Median age of diagnosis is 70 for males and 74 for females.
- Typical frontline treatment: multiagent systemic therapy (e.g. fludarabine – cyclophosphamide – rituximab [“FCR”], bendamustine - rituximab [“BR”])
- Ibrutinib (first in class kinase inhibitor of BCR signaling) approved in 2014
  - > Treatment of patients with CLL who have received at least one prior therapy and patients with CLL with 17p deletion, irrespectively of the line of therapy.
  - > Majority of responses to ibrutinib are partial
- HLA-E is expressed in virtually all patients with CLL, at higher levels compared to normal B cells (Veuillen, Aurran-Schleinitz et al. 2012).
- Ibrutinib creates a favorable pro-inflammatory environment; this could result in a synergistic effect with the immunotherapeutic action of monalizumab.

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OTHER ASSETS & TECHNOLOGY

IPH33, PROPRIETARY PRECLINICAL ASSET
A BLOCKING MAB TARGETING TLR3

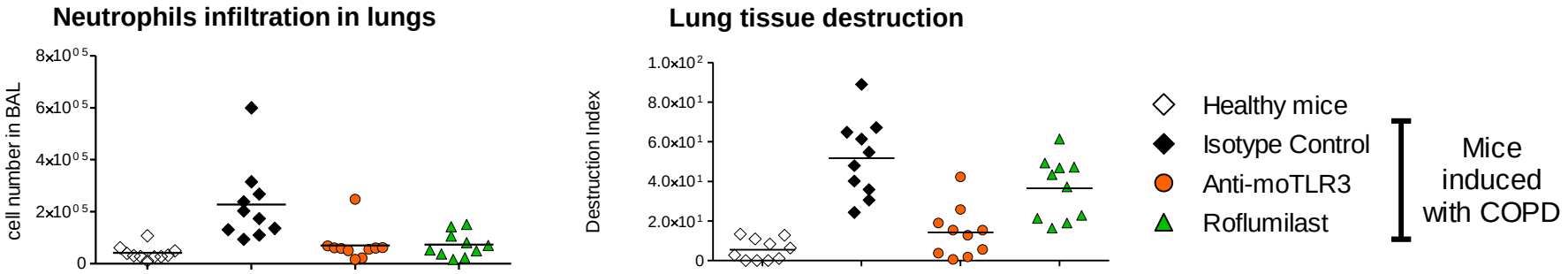
- Blocking TLR3 aims at preventing inflammatory cytokine production, upstream of current treatments for inflammation
  - > Major inducer of type I IFN and inflammatory cytokines (IL-6, TNF)
  - > Overexpressed on inflammatory epithelial cells
- Innate Pharma's humanized anti-TLR3 antibodies:
  - > Are specifically internalized in TLR3-expressing cells and show efficient blocking of TLR3 signaling, with high potency
  - > Surrogate anti-mouse TLR3-blocking antibody shows activity in murine models of COPD and IBD
  - > This activity compares favorably to approved anti-inflammatory agents
- One mAb program from J&J/Centocor against TLR3 in Phase I trial
  - > Differentiated IP estate

Broad spectrum of potential chronic inflammation pathologies

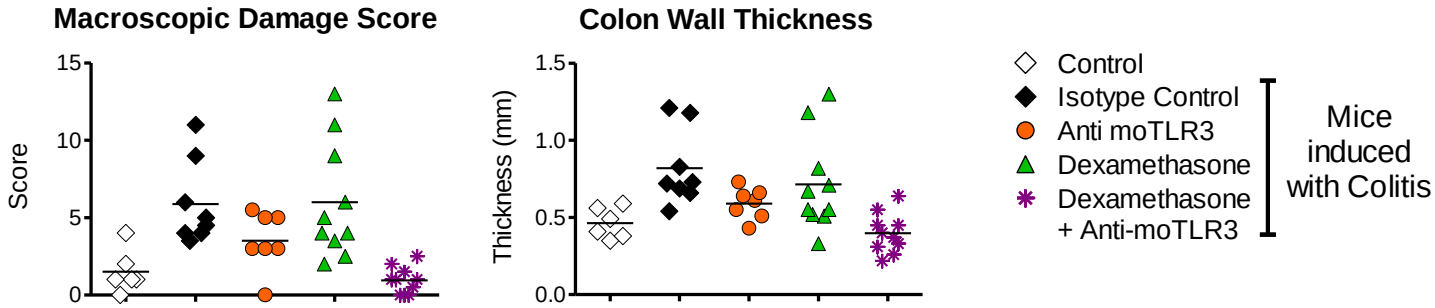
Currently in pre-clinical validation - **Next step: partnering**

IPH33, PROPRIETARY PRECLINICAL ASSET
A BLOCKING MAB TARGETING TLR3

- Mouse model of LPS+Elastase induced COPD



- Mouse model of TNBS induced colitis



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Discovery, anti-CD39

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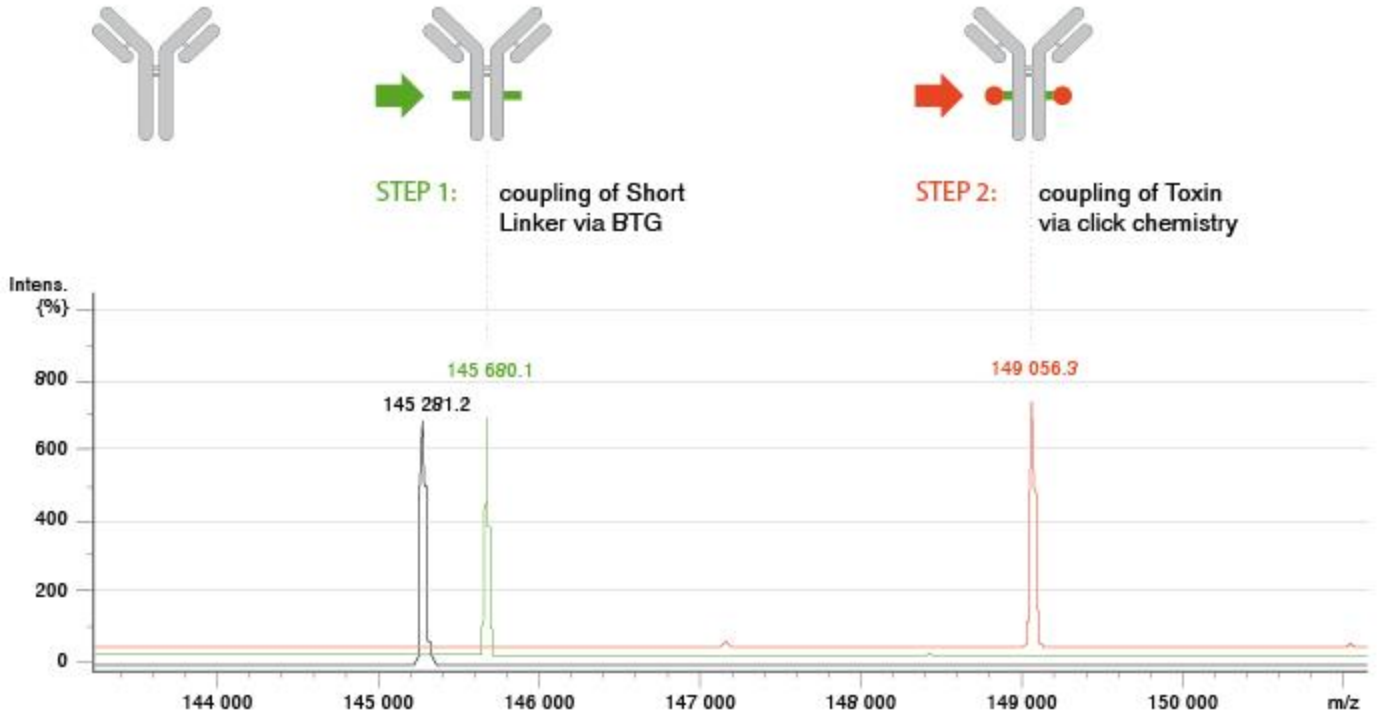
PROPRIETARY ANTIBODY-DRUG CONJUGATES TECHNOLOGY

SITE-SPECIFIC CONJUGATION TECHNOLOGY FOR HOMOGENOUS ADC

- New site-specific conjugation technology using bacterial transglutaminase (BTG) enzyme on an minimally modified antibody scaffold (single point mutation)
- ADCs with DAR of exactly 2:1 or 4:1

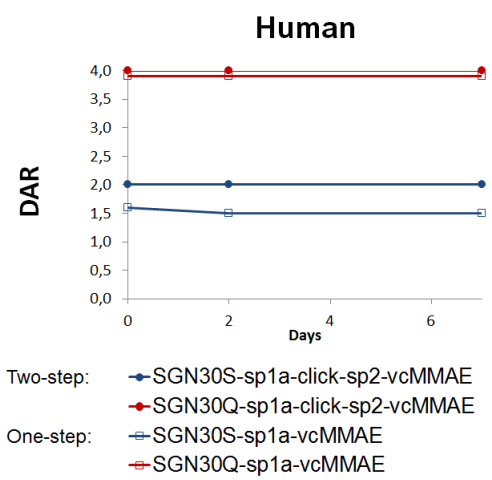


PROPRIETARY ANTIBODY-DRUG CONJUGATES TECHNOLOGY

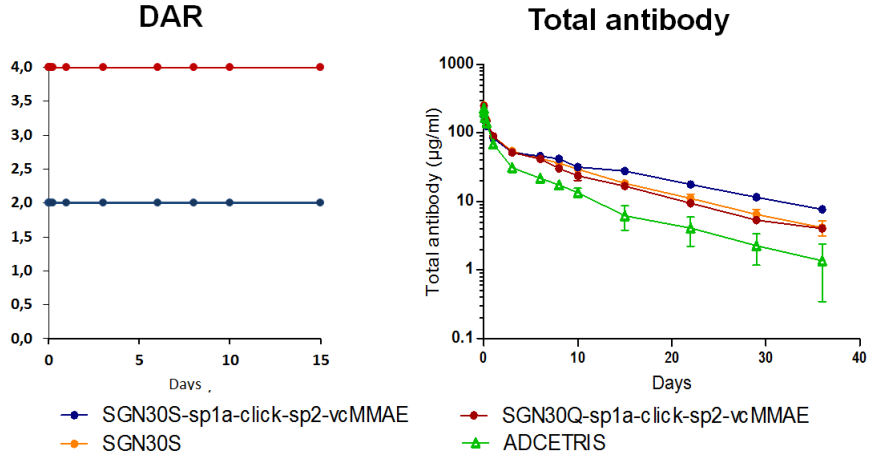
SITE-SPECIFIC CONJUGATION TECHNOLOGY FOR HOMOGENOUS ADC

- Stability *ex vivo* in human and cynomolgus plasma over one week
- Stability and favorable pharmacokinetics in rat over 2 weeks
- Efficacy validated in preclinical models

Stability in Plasma Over One Week



Pharmacokinetics in Rat

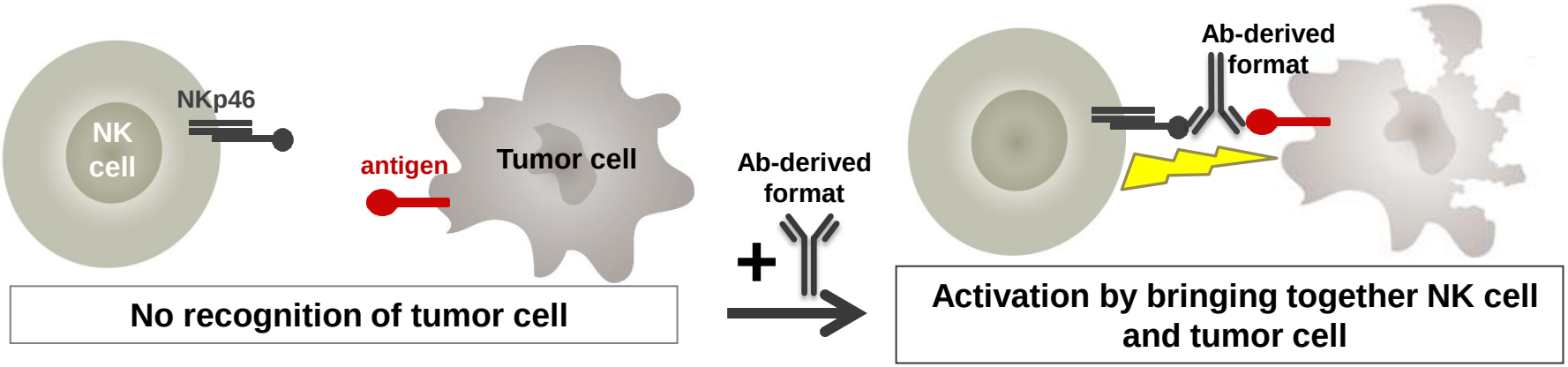


May be used for a broad spectrum of target antigens and can accommodate both existing and future high potency toxins

New opportunities for portfolio expansion and partnering (e.g. Sanofi collaboration)

BISPECIFIC ANTIBODY TECHNOLOGY ENGAGING NK CELLS

- Innovative bispecific antibody technology for engaging NK cells to kill tumor cells through NKp46
- NKp46 is an activating receptor expressed on all NK cells
- NKp46-bispecific NK cell engagers brings tumor cells and NK cells together and trigger NK cell degranulation and tumor cell destruction



New opportunities for proprietary portfolio expansion and partnering

Research collaboration and licensing agreement with Sanofi

- Up to two bispecific candidates using technology from IPH and Sanofi's proprietary bispecific antibody format as well as tumor targets
- IPH is eligible to up to €400m in development and commercial milestone payments as well as royalties on net sales