innate pharma

Building a leading oncology company focused on innate immunity

London
July 13, 2016

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FORWARD LOOKING STATEMENT

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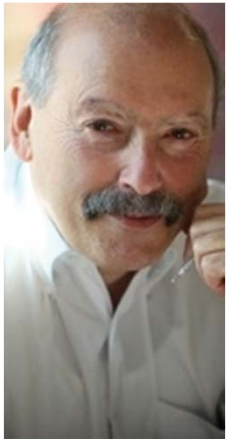
Novartis, Aventis



Marcel
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President, Innate Pharma Inc.

BMS

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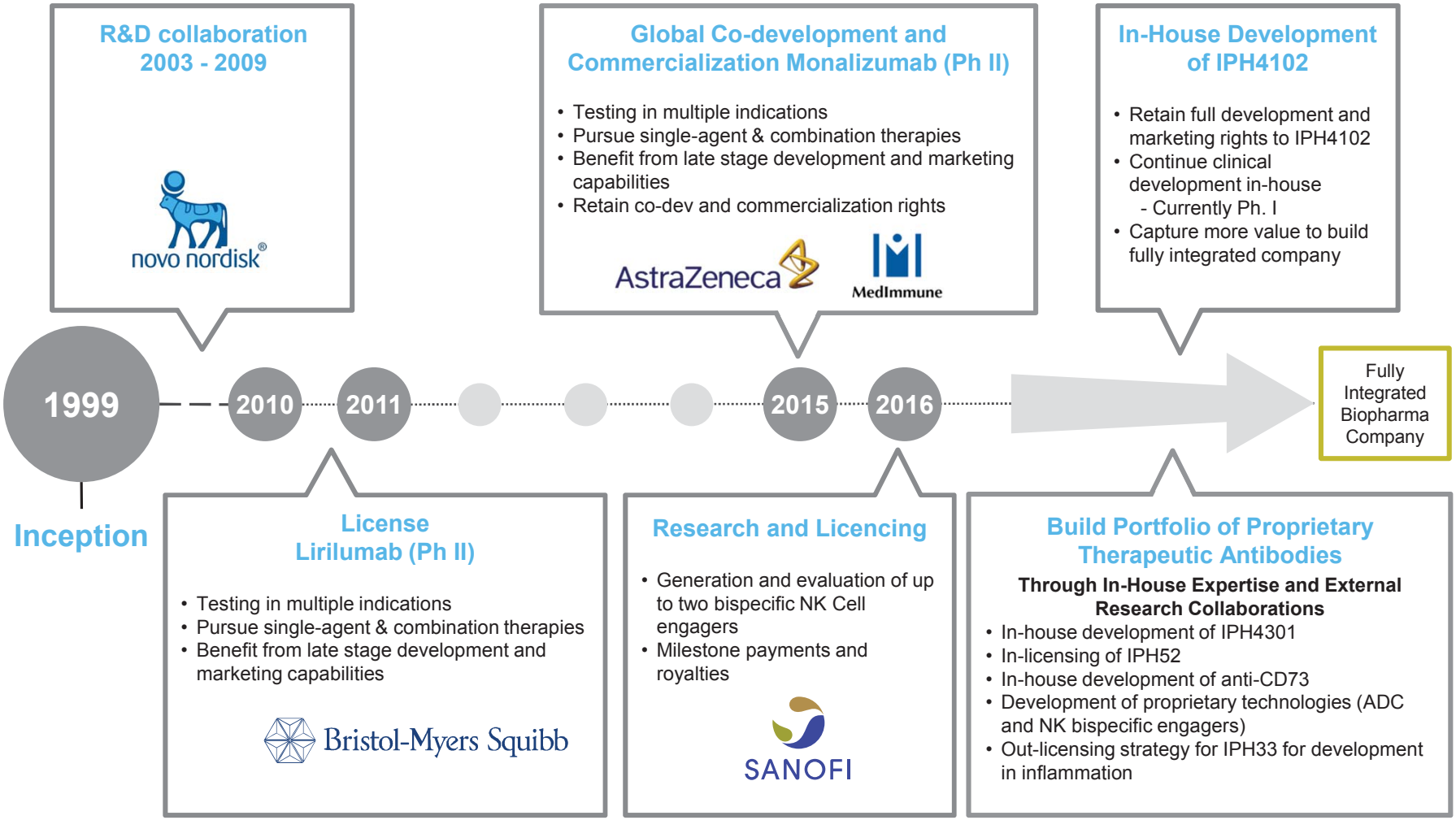
PhD,
Chief Development Officer
Pasteur Merieux Sangstat

BUILDING A LEADING ONCOLOGY COMPANY FOCUSED ON INNATE IMMUNITY

Differentiated and Novel Science in Immuno-Oncology	• Pioneer of the innate immune system and NK cell biology • Highly productive R&D organization
Portfolio of First-in-Class Antibodies	• 3 clinical stage candidates addressing novel targets, including two differentiated checkpoint inhibitors • Proprietary antibody platform (Bispecifics and ADCs)
Partnerships with Leading Immuno-Oncology Companies	• Bristol-Myers Squibb (Lirilumab) • AstraZeneca (Monalizumab) • Sanofi (NK Bispecific Engagers)
Strategy to Become a Fully Integrated Biopharma Company	• Retained co-dev/commercialization rights to monalizumab and full rights to IPH4102 • Leveraging late-stage development and marketing capabilities of partners
Strong Financial Position and Management Team to Execute on the Business Plan	• ~€700MM market cap, traded on the Euronext • 1Q2016 cash at €255,8M • Significant clinical catalysts expected in 2016 and 2017

STRATEGY TO BECOME A FULLY INTEGRATED BIOPHARMA COMPANY



DEVELOPING A BROAD AND DIVERSIFIED ANTIBODY PORTFOLIO WITH NOVEL MECHANISMS OF ACTION

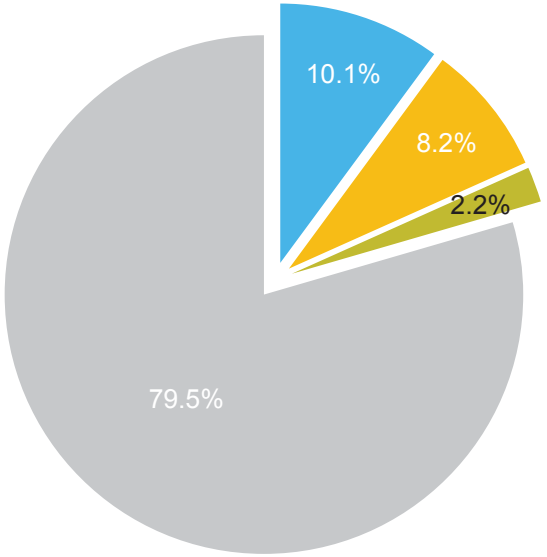
PROGRAM	TARGET	INDICATION	STAGE
Lirilumab Licensed to Bristol-Myers Squibb	KIR2DL1,2,3	Acute Myeloid Leukemia - Single agent Solid and hematological tumors - Multiple combinations	Phase II 6 Phase I & II trials
Monalizumab Co-development with AstraZeneca	NKG2A	Solid and hematological tumors - Single agent and multiple combinations	5 Phase I/II trials
IPH4102	KIR3DL2	Cutaneous T-cell lymphomas	Phase I
IPH4301	MICA/B	Cancer	Research
IPH52	CD39	Cancer	Research
Discovery	CD73	Cancer	Research
IPH33	TLR3	Inflammation	Research

TECHNOLOGY	
NK bispecific engagers	Collaboration with Sanofi; up to two engagers on two undisclosed tumor targets
Antibody Drug Conjugate (ADC)	

SHARE CAPITAL
KEY FIGURES AND ANALYST COVERAGE

Well capitalized with cash, cash equivalents, and financial instruments of €255.8 million at the end of 1Q16**

- Listed on Euronext, IPO in November 2006
  - > Euronext Paris: FR0010331421 – IPH
- Stock liquidity (in 2016)
  - > 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*

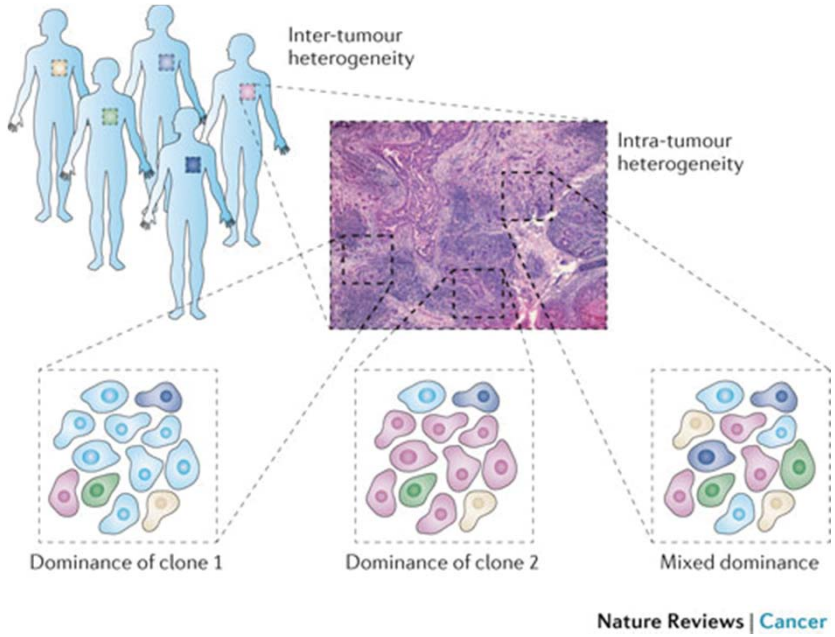
***Including short term investments (€51.2m) and non-current financial instruments (€37.5m).*

INNATE PHARMA'S R&D STRATEGY AND APPROACHES IN IMMUNO-ONCOLOGY

IMMUNO-ONCOLOGY: A REVOLUTION IN CANCER TREATMENT

NEED FOR CHECKPOINTS BEYOND PD-1

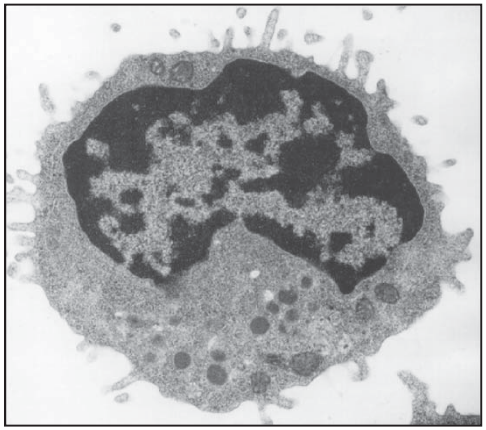
- IO can lead to profound and durable responses in subsets of patients
  - > Expected to impact all indications, all lines of treatments
- Led by checkpoint inhibitors, that “release the brake” on T cells
- But many patients fail to respond optimally
  - > ~70-80% non-responders in head&neck, renal, lung, breast, and gastric cancer...



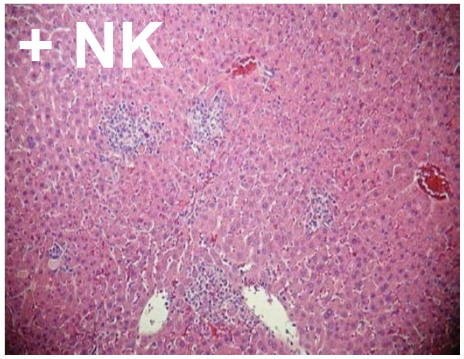
- Patient stratification
- Combination therapy
- New drugs with new MOAs

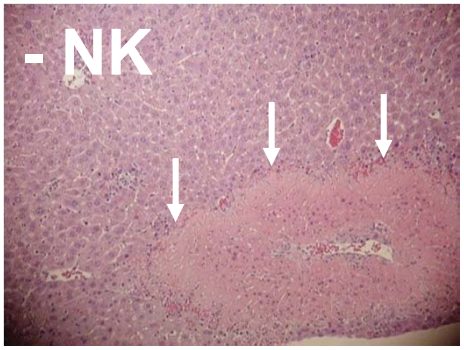
INNATE PHARMA'S PLATFORM

COUNTERACT TUMOR ESCAPE BY BOOSTING NATURAL KILLER CELLS



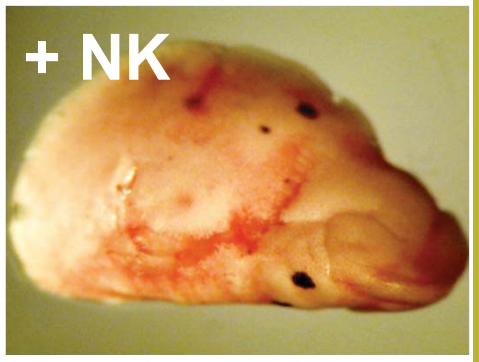
Virus

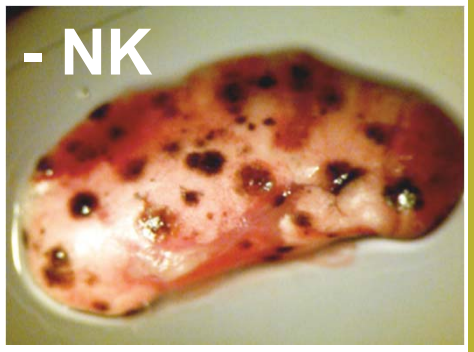




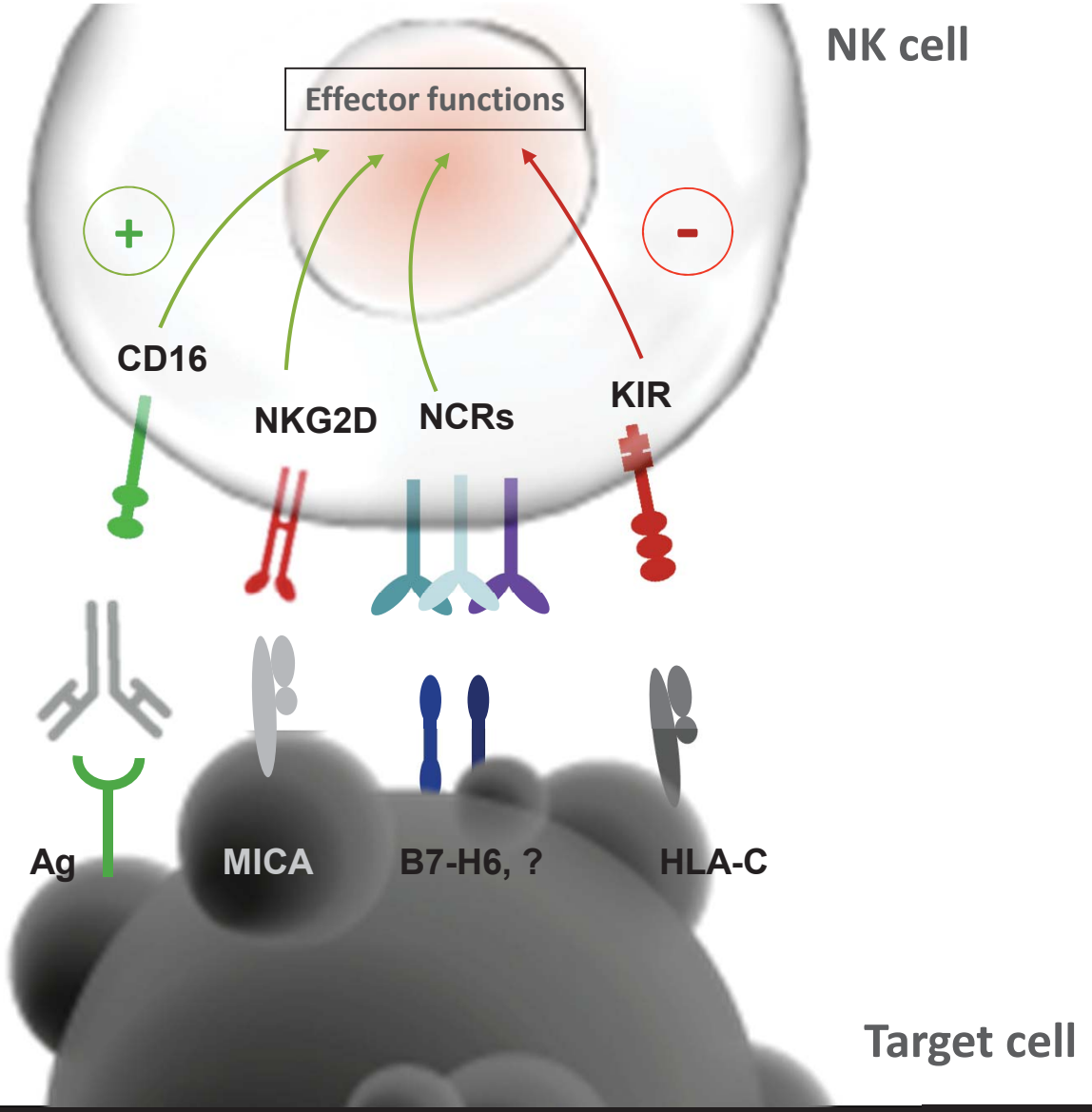
- Provide rapid, first-line defense
- Directly kill tumors and virus-infected cells
- Produce cytokines (e.g. IFN-y) that are critical for adaptive T cell responses
- Important role in controlling metastasis

Tumors





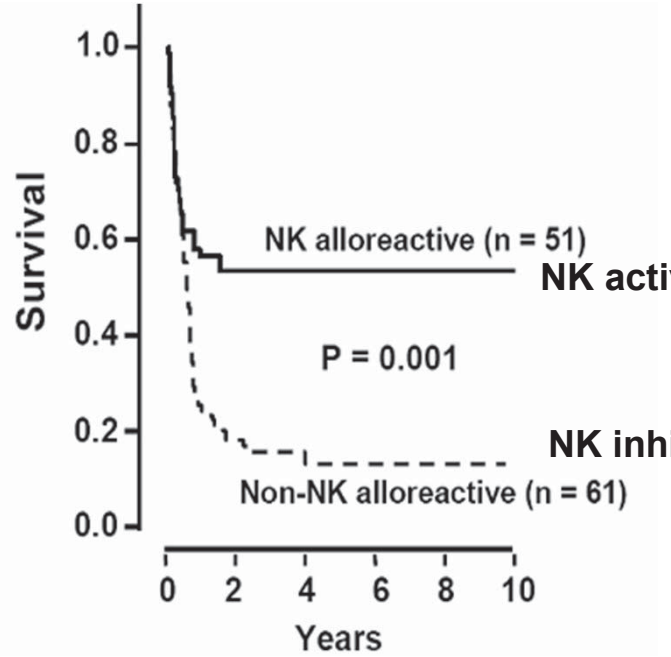
NK CELLS ARE CONTROLLED BY ACTIVATING AND INHIBITORY RECEPTORS



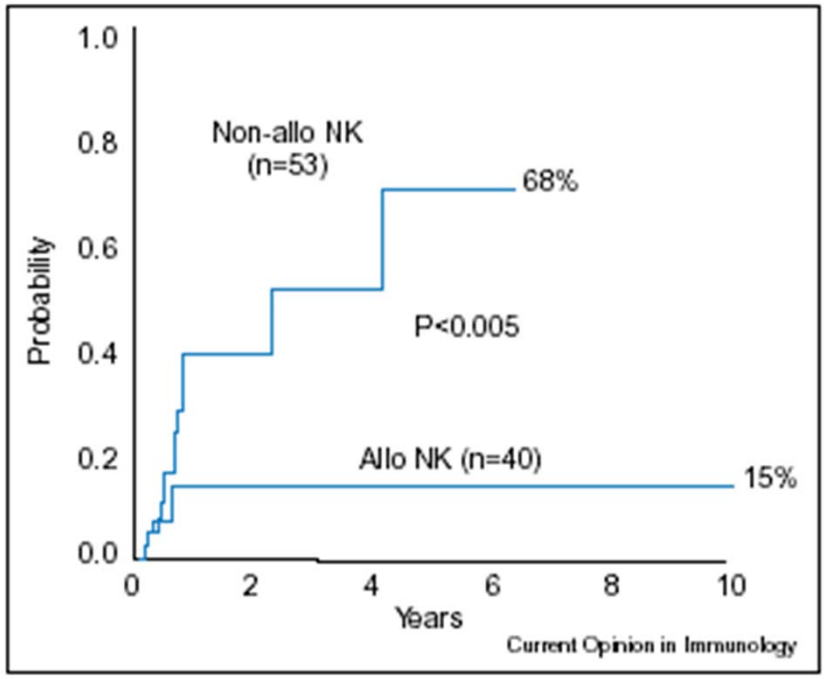
THERAPEUTIC POTENTIAL OF NK CELLS REVEALED IN AML
KIR TARGET VALIDATION

- NK cells can improve survival in AML (Acute Myeloid Leukemia) patients receiving haplo-identical stem cell transplantation: **Effects are durable and safe**

Survival

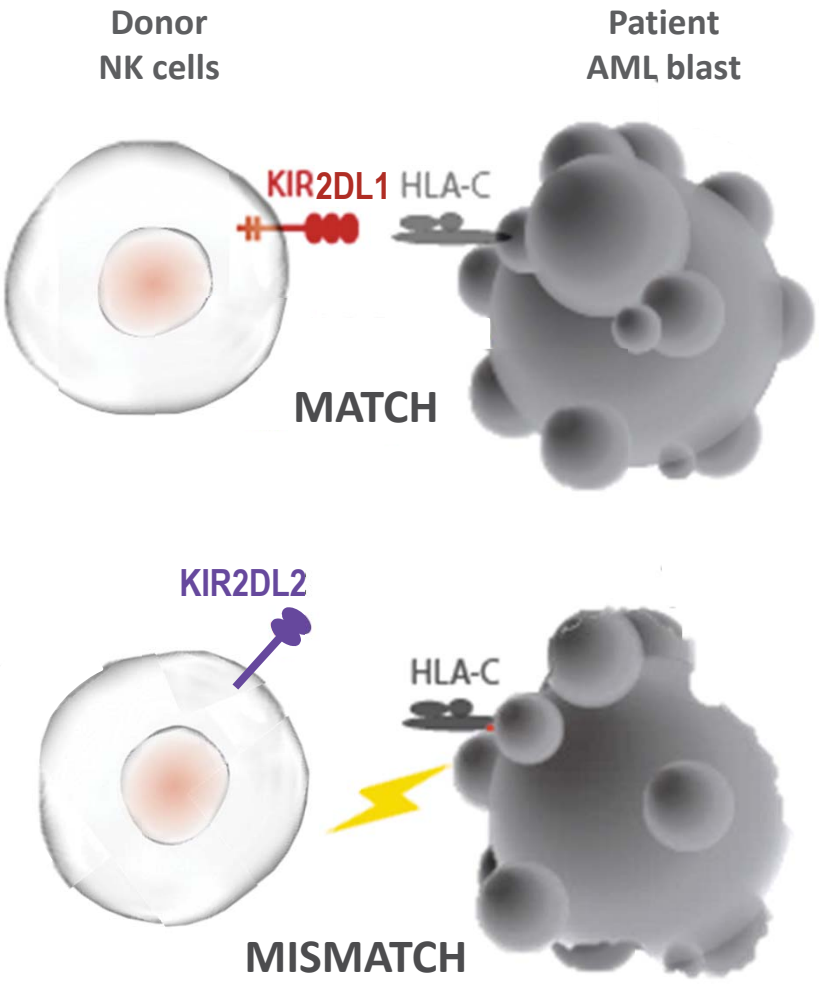


Relapse



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

FROM ALLO-TRANSPLANTATION TO DRUG

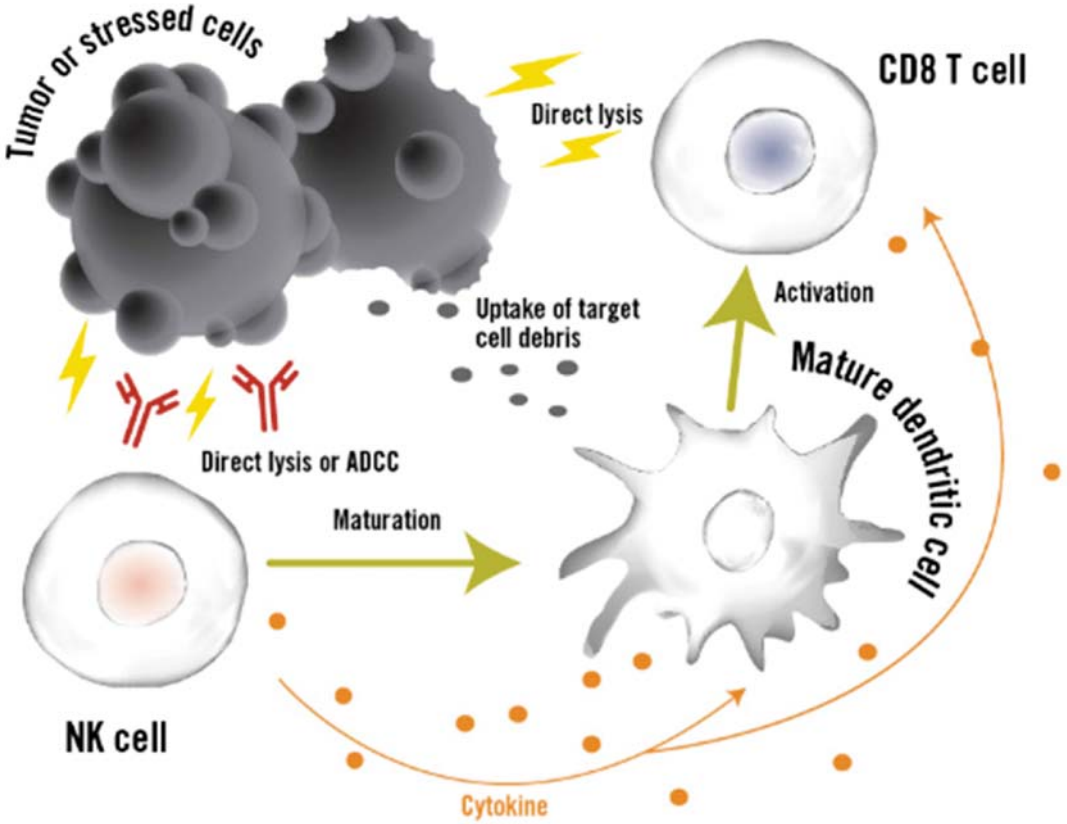


KIR INHIBITION

NO KIR INHIBITION: KILLING

Therapeutic targeting required a panKIR2DL mAb: Lirilumab

NK CELL ANTI-CANCER FUNCTIONS



- **Natural cytotoxicity:**
  - > Provide early control by directly killing tumors
- **Cytokine production:**
  - > Stimulate adaptive immune response, by secreting cytokines, e.g. GM-CSF that stimulates dendritic cells and IFN-γ and IL-2 that stimulates T cells
- **Roles in memory responses:**
  - > Antibody-dependent cytotoxicity
  - > Increasing evidence that NK cells can be educated, generating long-term memory NK cells

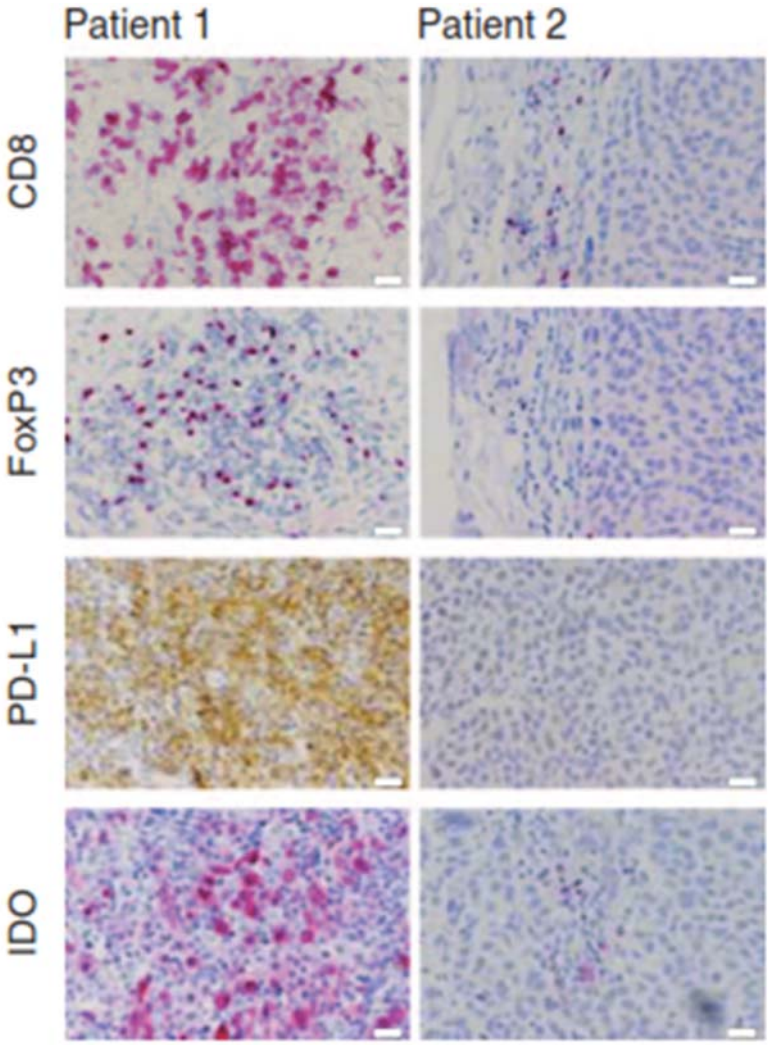
Adapted from Vivier et al., Nature Immunology 2008, Vivier et al., Science 2011

OUR STRATEGY BEYOND PD-1

Our strategy for PD-1 non- or partial-responders with inflamed phenotype:

Combination treatment with NK checkpoint mAbs

mAbs targeting suppressive microenvironment



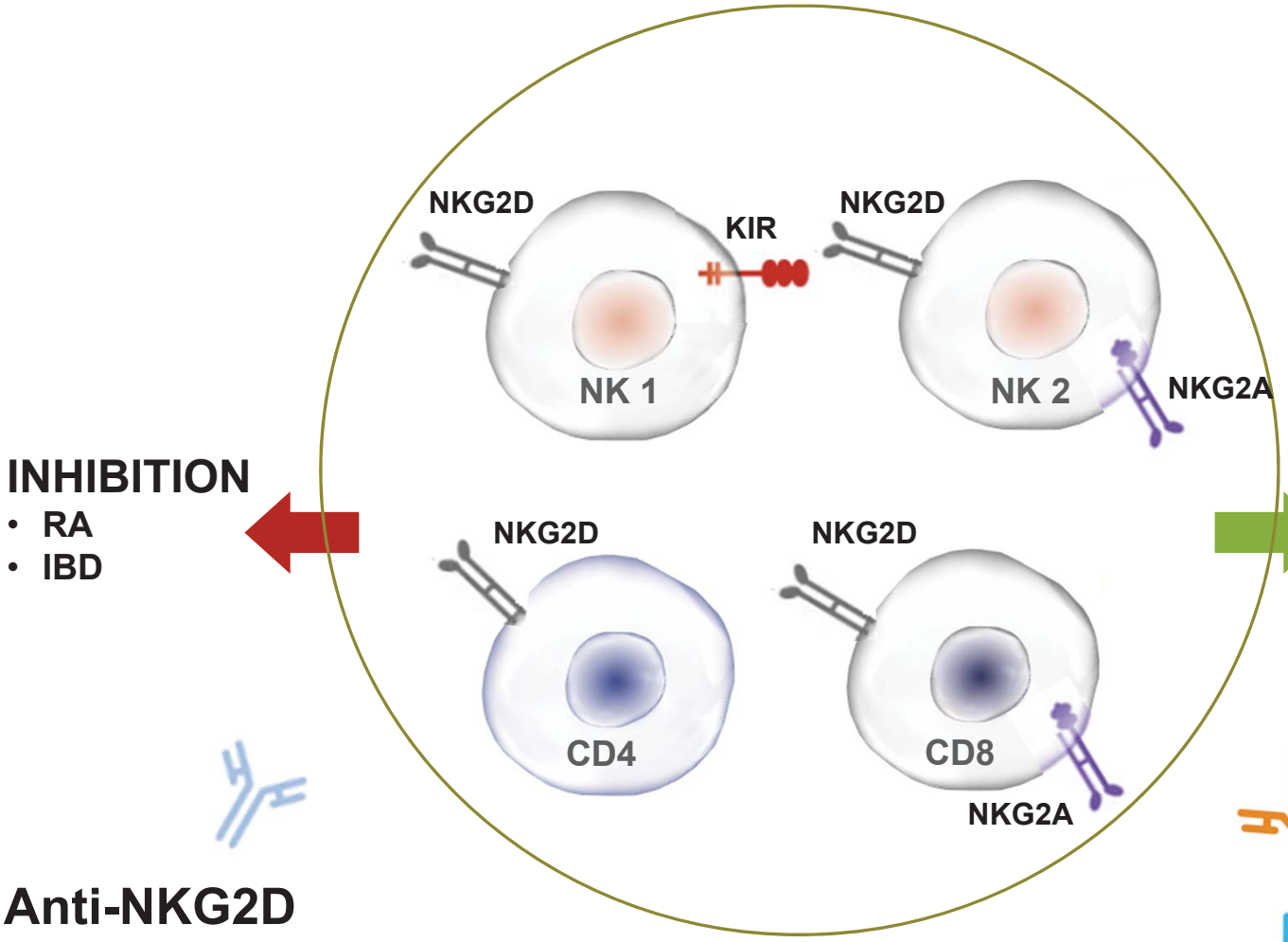
Spranger et al. Science Translational Medicine 2013

Our strategy for patients with non-inflamed tumors:

Bispecifics that trigger NK cells, to kill and to provide an innate boost, eg GM-CSF, IFN-□ □ to activate and recruit DCs and T cells

DIFFERENT NK SUBSETS EXPRESS DIVERSE RECEPTORS

"NK RECEPTORS" CAN ALSO BE EXPRESSED BY T CELLS



INHIBITION
- RA
- IBD

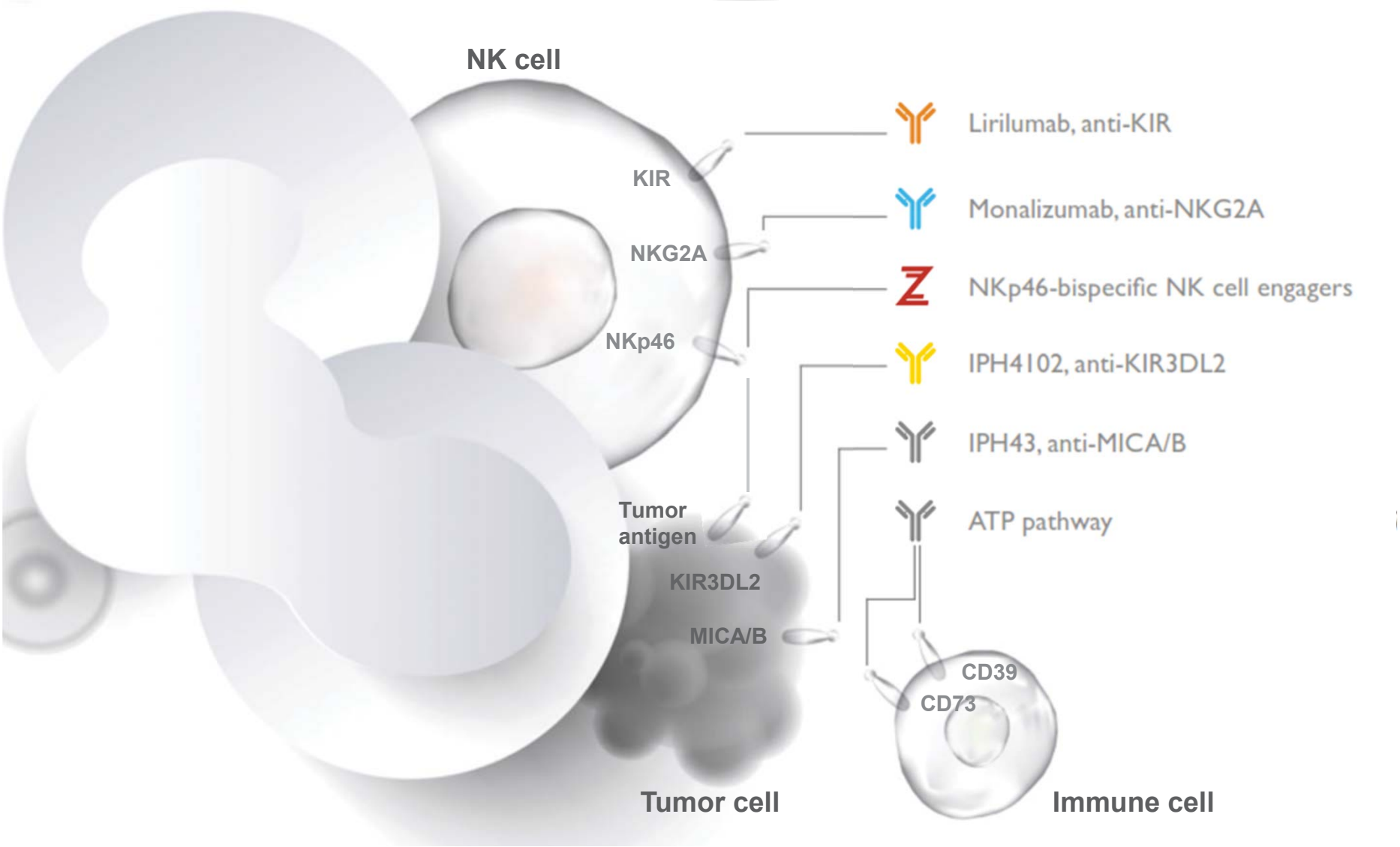
ACTIVATION
- Solid Tumors
- Hemato-oncology
- Infection

Anti-NKG2D

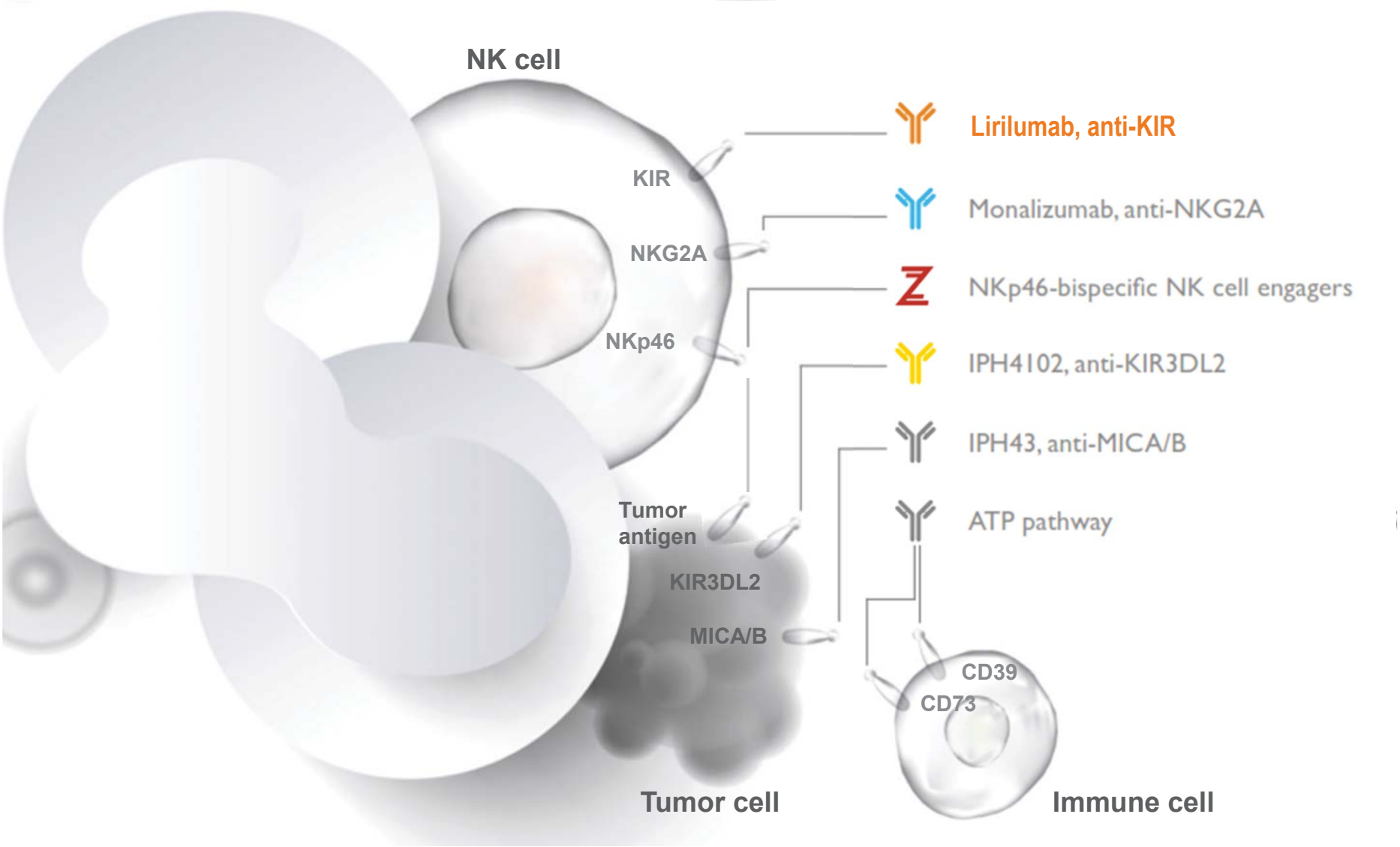
Anti-KIR

Anti-NKG2A

INNATE PHARMA'S PIPELINE
TARGETING CHECKPOINTS IN IMMUNO-ONCOLOGY

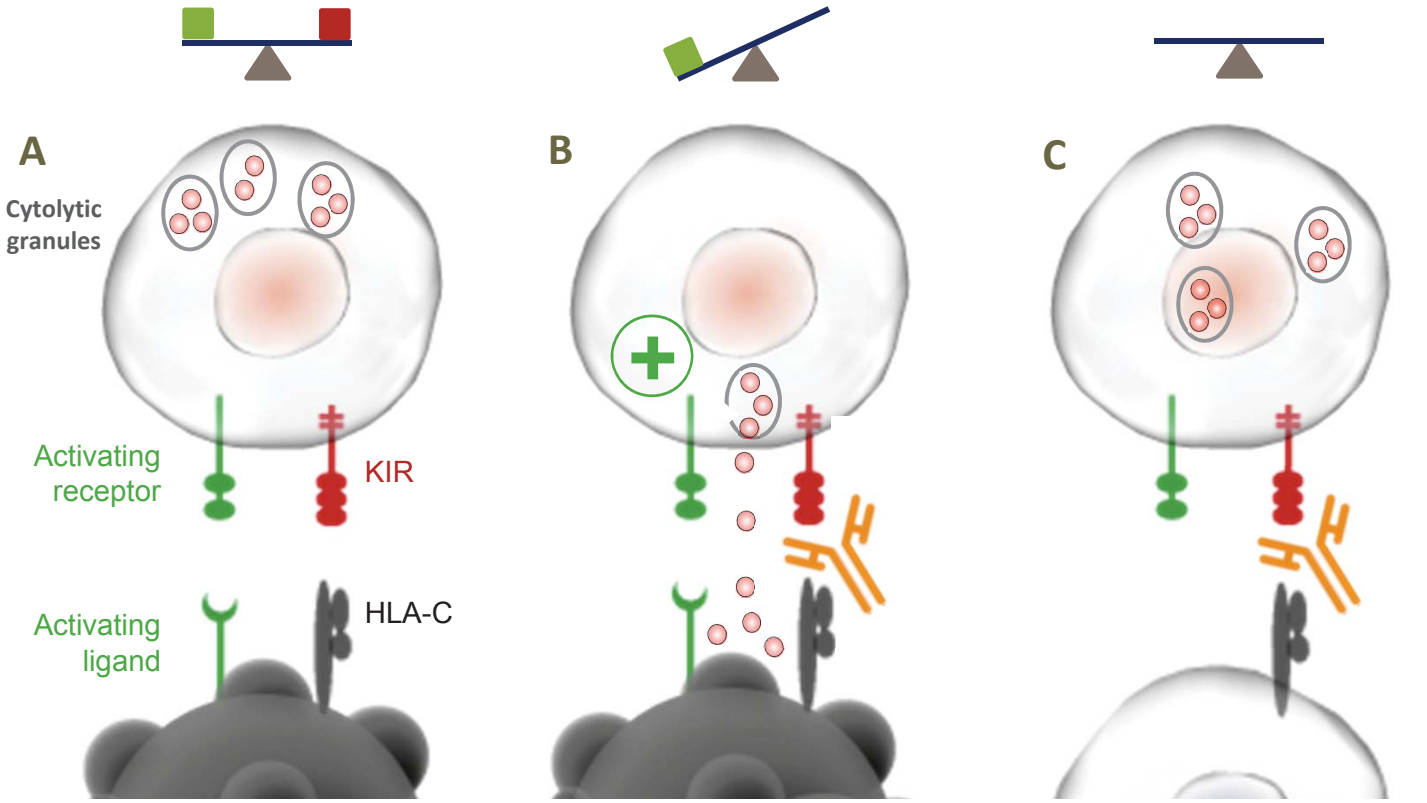


LIRILUMAB, FIRST-IN-CLASS ANTI-KIR MAB
LICENSED TO BRISTOL-MYERS SQUIBB



LIRILUMAB IS A FIRST-IN-CLASS KIR CHECKPOINT INHIBITOR

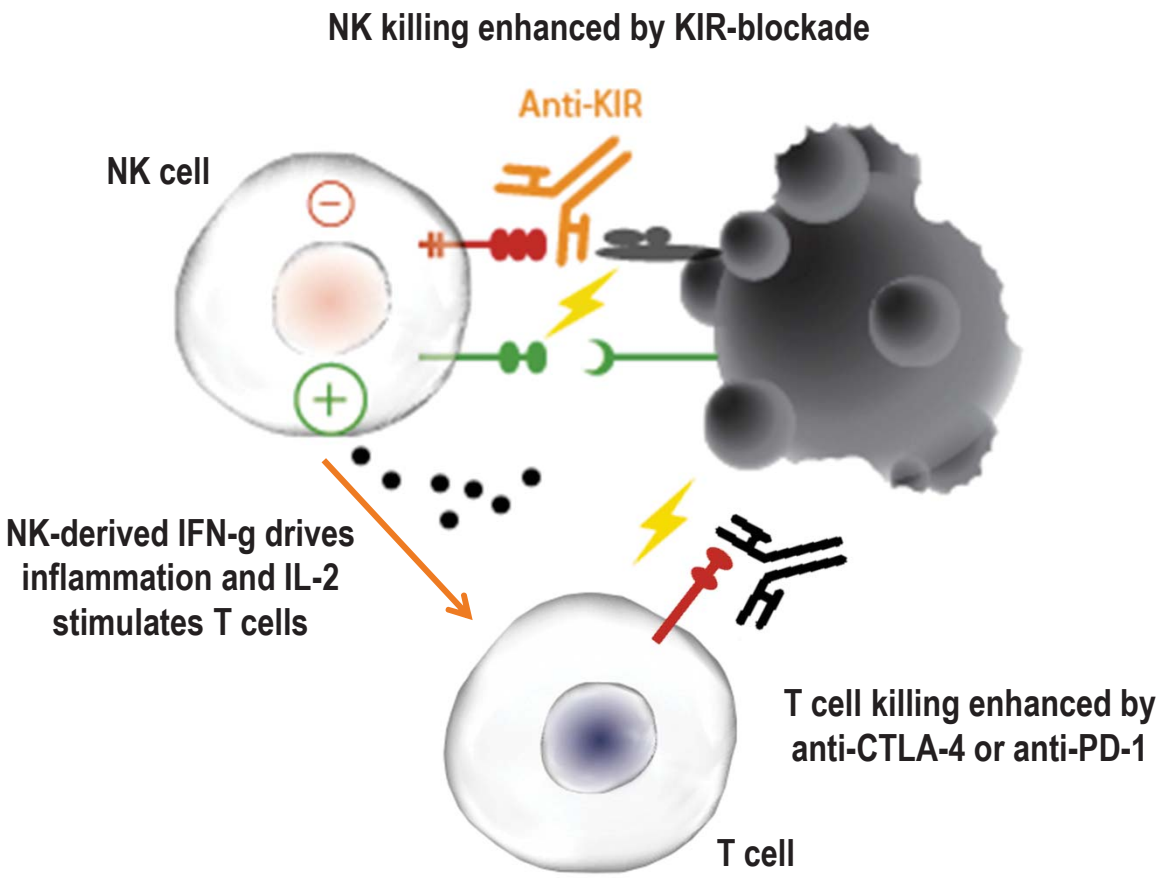
MECHANISM OF ACTION



Tumor cell expressing activating ligand	Tumor cell expressing activating ligand	Normal cell not expressing activating ligand
No kill	**Kill**	**No kill** **No autoimmunity**

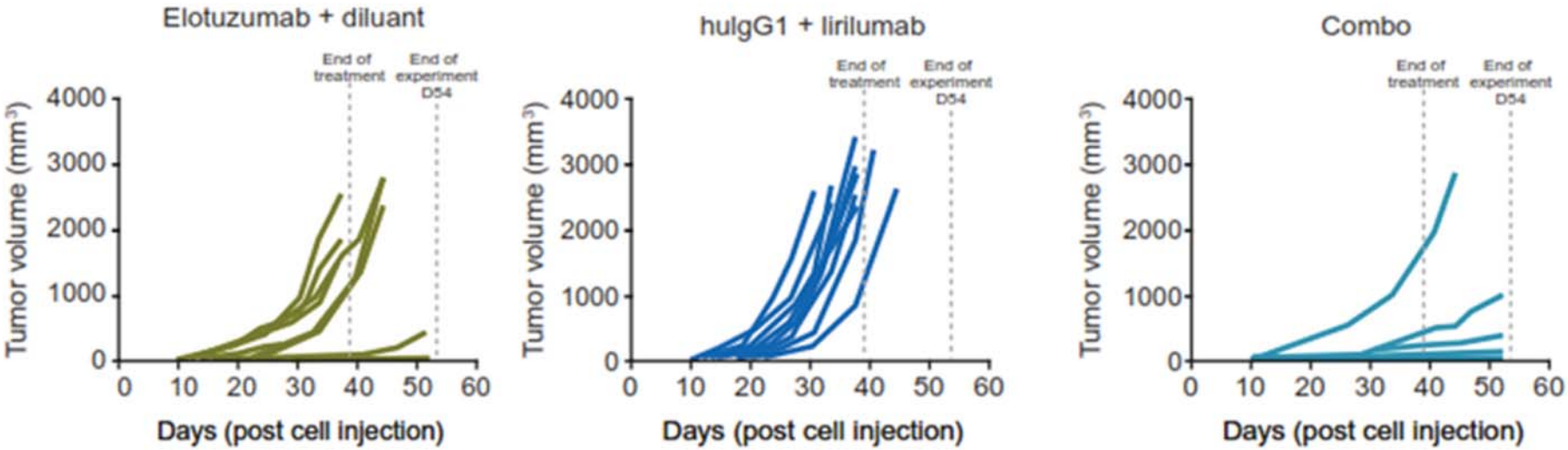
RATIONALE FOR LIRI – NIVO COMBO TRIALS

NK CELLS KILL TUMORS DIRECTLY, AND HELP T CELLS



NK CHECKPOINT RECEPTORS INHIBIT ADCC
DEMONSTRATION IN *IN VIVO* ASSAYS

***In vivo* effects of KIR blockade (lirilumab) on elotuzumab activity in xenograft tumor model**[1]

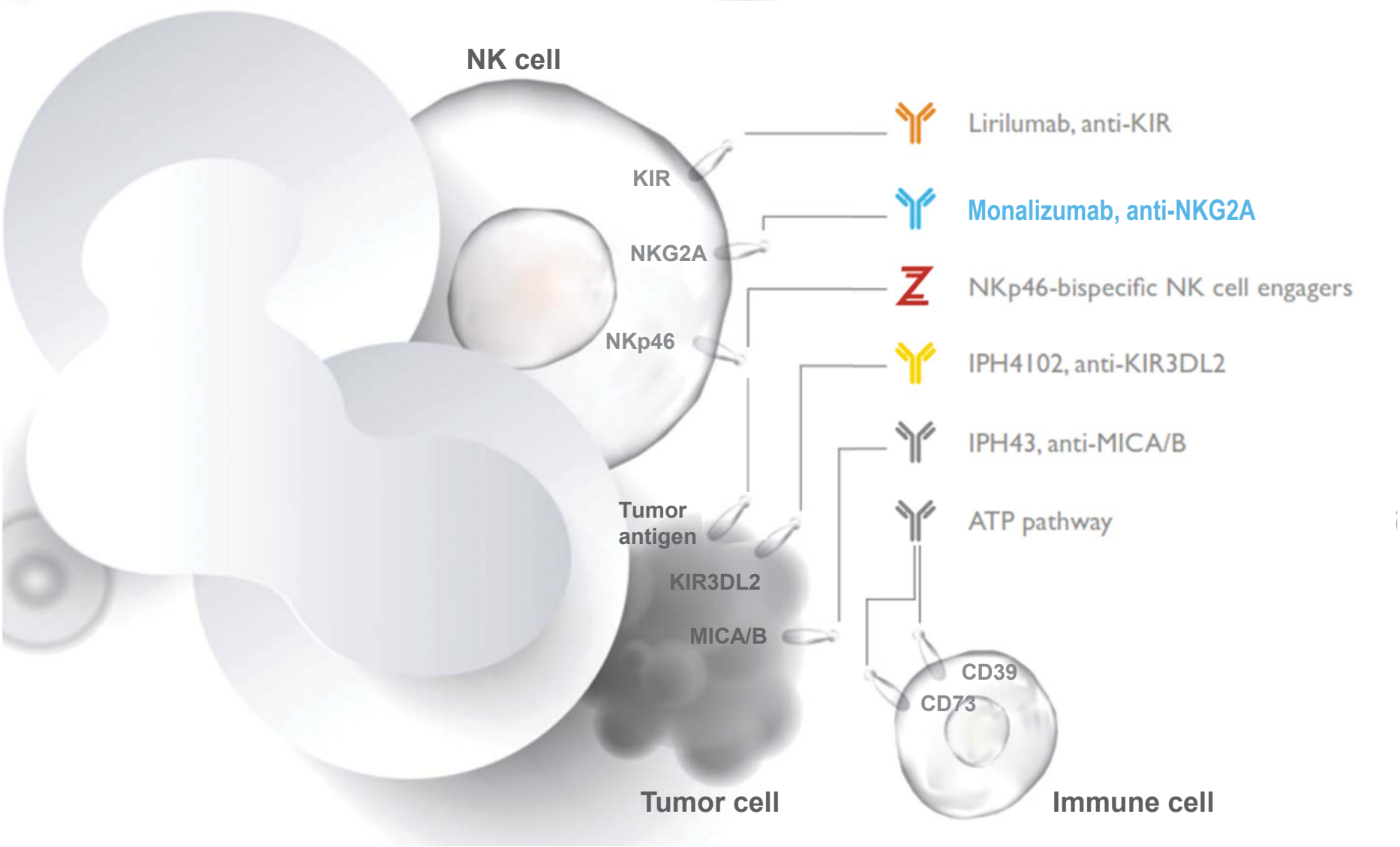


- Similarly, ADCC by anti-CD20 and anti-EGFR is enhanced by combining with anti-KIR or anti-NKG2A[2]

1. Robbins et al., ASH 2014 poster; Sola et Al., ASH 2014 poster;
2. Kohrt et al., Blood, 2014; Internal data

MONALIZUMAB IPH2201, FIRST-IN-CLASS ANTI-NKG2A MAB

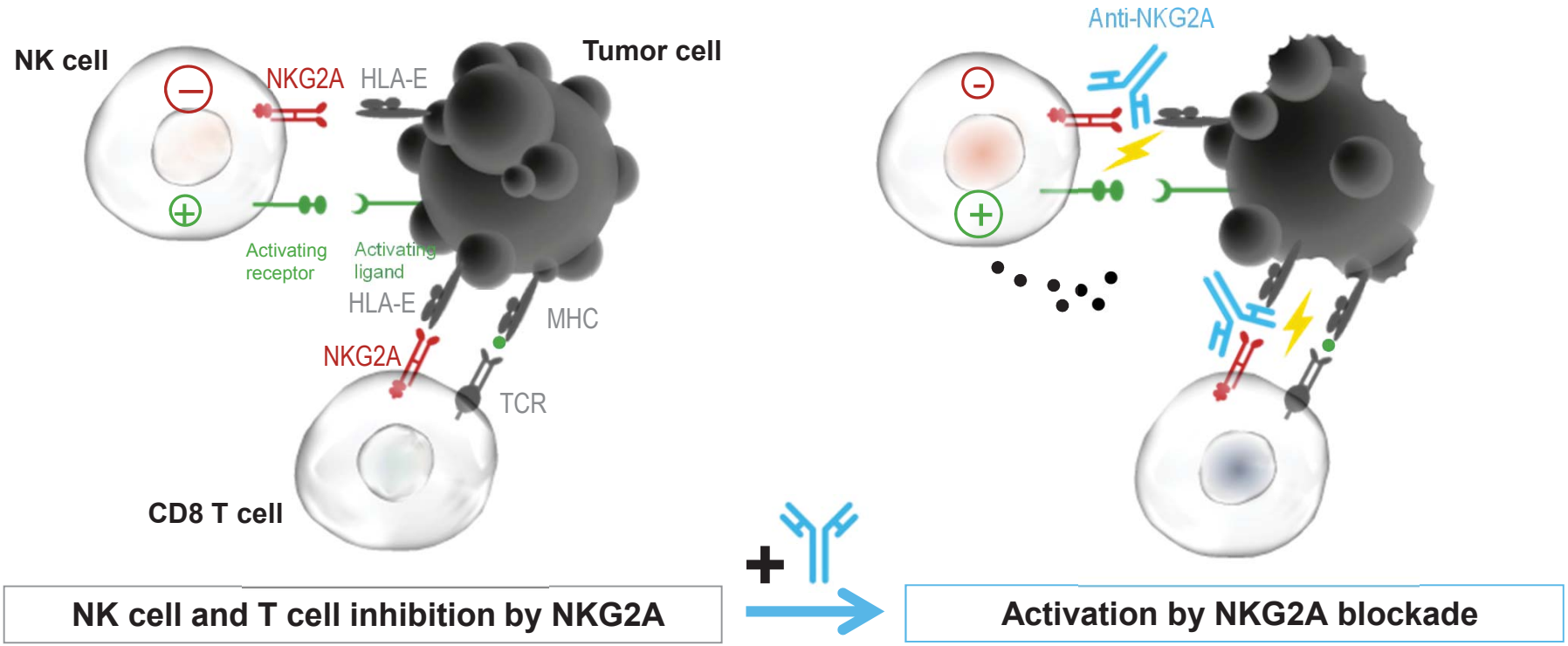
CO-DEVELOPMENT AND COMERCIALIZATION AGREEMENT WITH ASTRAZENECA



MONALIZUMAB IS A FIRST-IN-CLASS NKG2A CHECKPOINT INHIBITOR

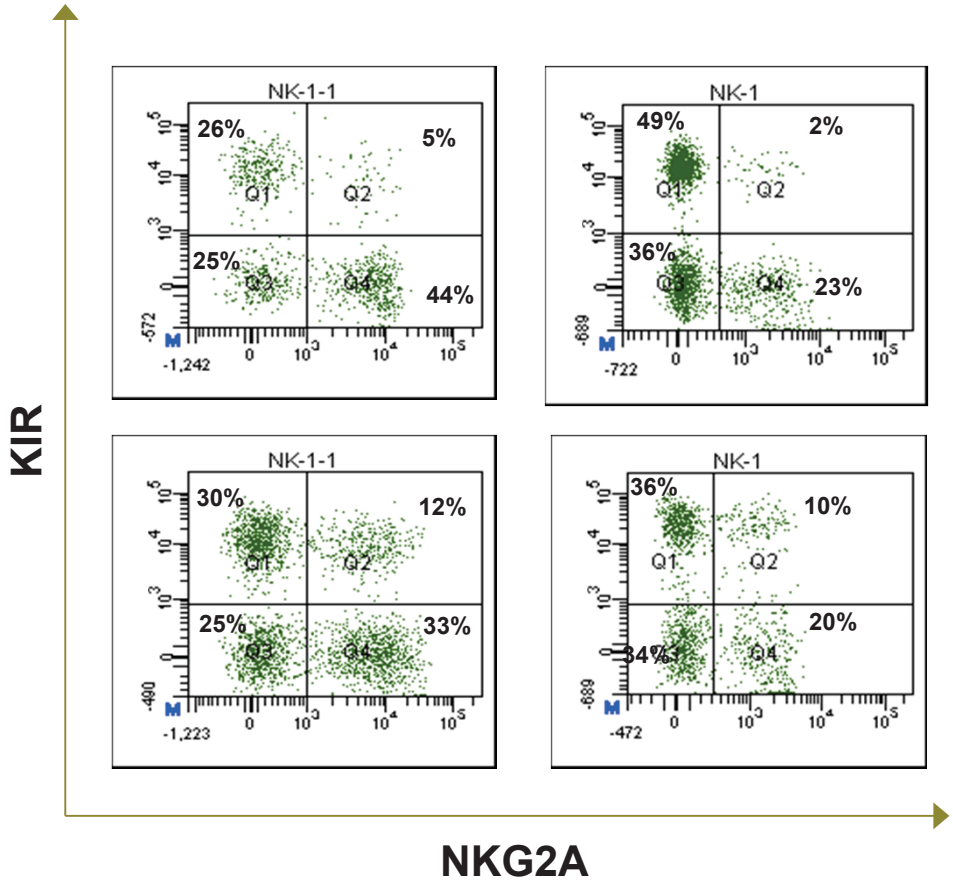
MECHANISM OF ACTION

- NKG2A is an inhibitory receptor on tumor infiltrating CD8 T cell and NK cells
- Prevents interaction with HLA-E molecules to potentiate NK cells and CD8 T cells anti-tumor activity



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



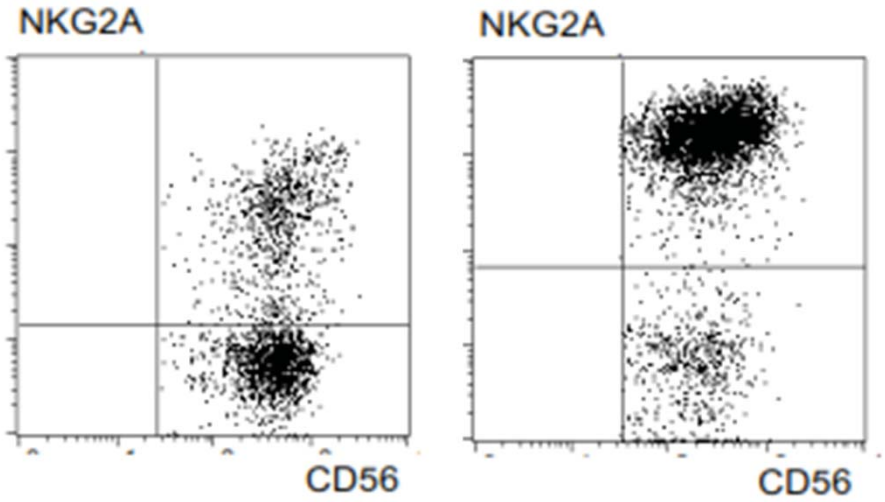
TUMOR INFILTRATING NK CELL MOSTLY EXPRESS NKG2A

NKG2A OFTEN INDUCED ON CD8+ T CELLS IN TUMORS

Accumulation of NKG2A+ NK cells inside tumors

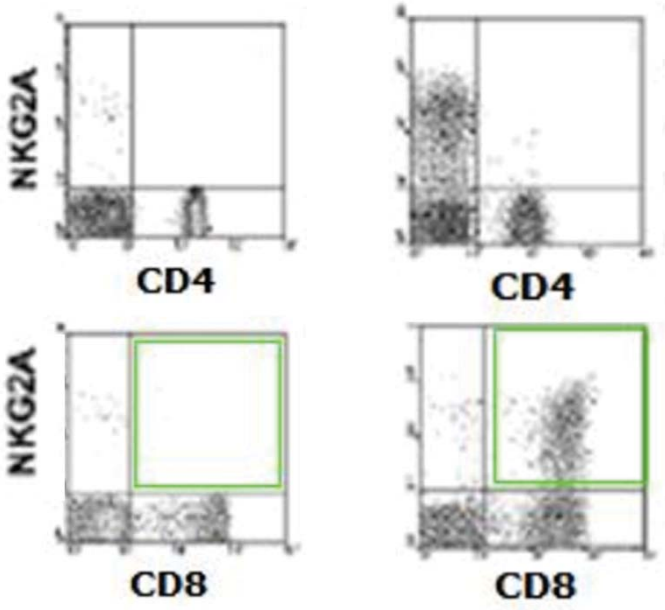
Induced expression of NKG2A on tumor infiltrating $CD8^+$ T cells

Lung carcinoma[1]



Blood NK (HC) **Intratumoral NK**

Cervical cancer[2]

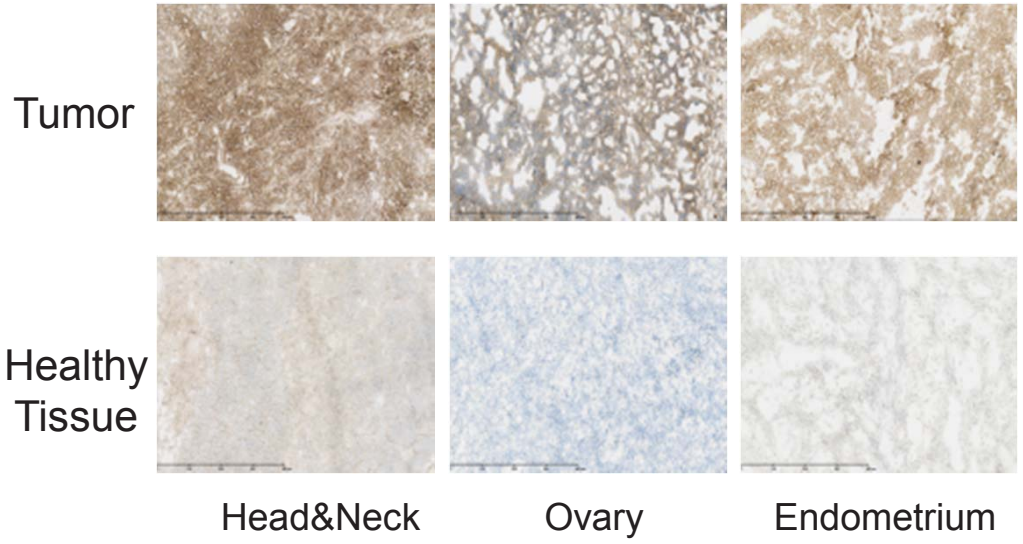


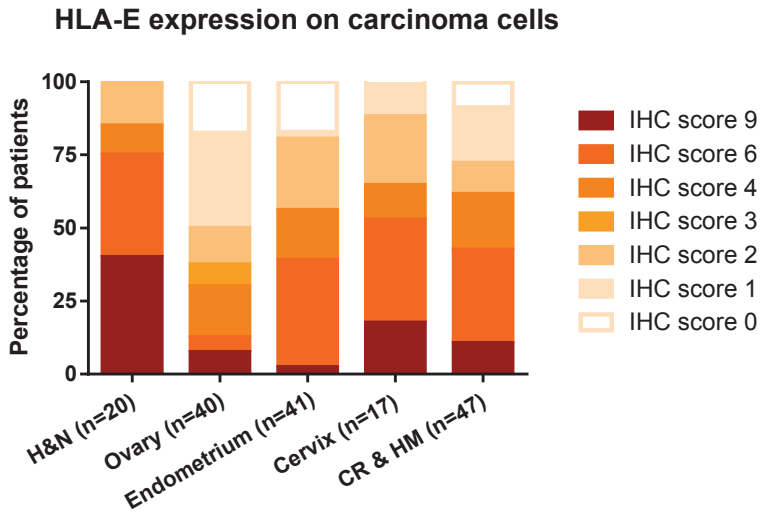
Blood T cell **Intratumoral T cell**

1. Platonova et al. Cancer Res 2011; 2. Sheu et al. Cancer Res 2005

MANY TUMORS OVEREXPRESS HLA-E, THE LIGAND OF NKG2A

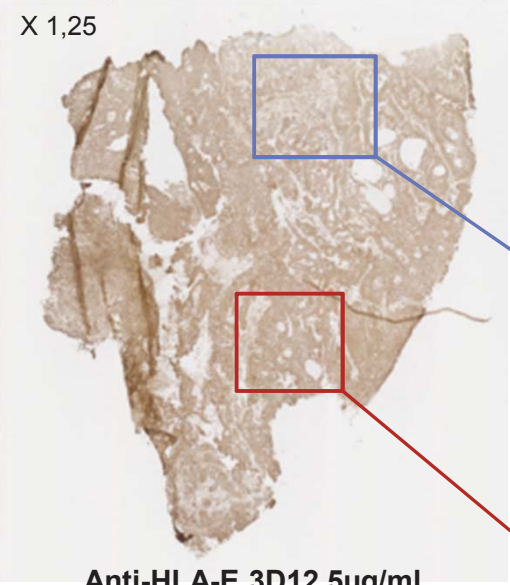
- HLA-E upregulated on a wide variety of tumor types:
  - > H&N, Ovarian, Endometrium, Colorectal, Cervix, Lung, Oesophagus, CLL
- Restricted expression on normal tissues
- Clinical development plan informed by expression of HLA-E





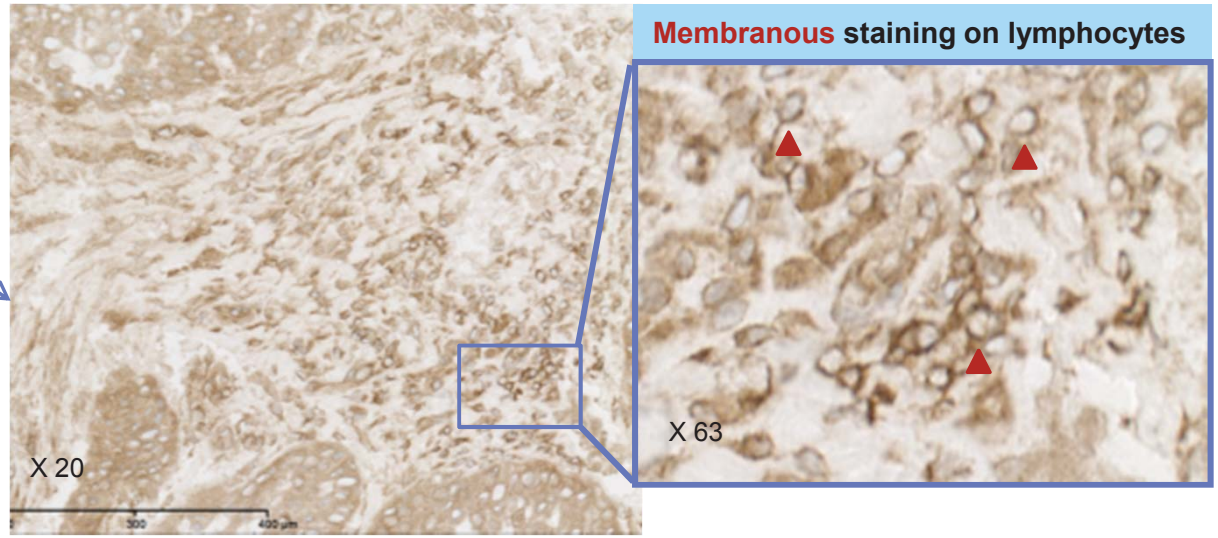
HLA-E EXPRESSION ON CARCINOMA CELLS AND LYMPHOCYTES

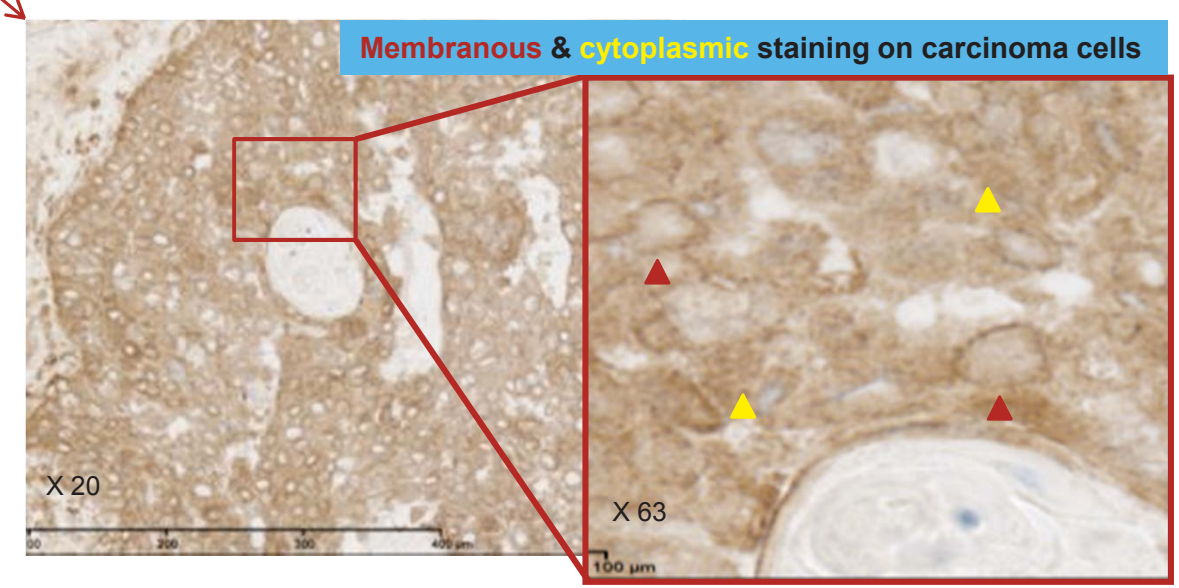
HEAD AND NECK TUMOR



Anti-HLA-E 3D12 5µg/ml

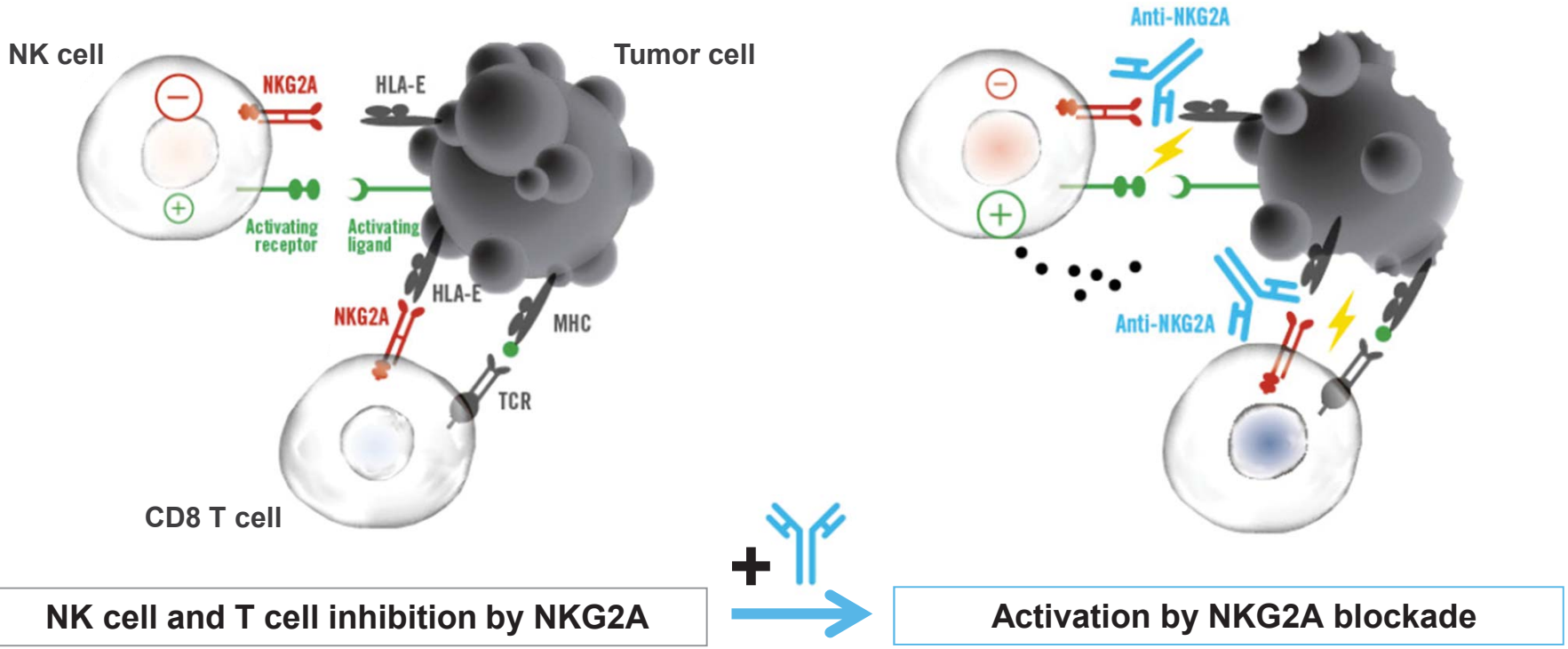
mIgG1 IC 5µg/ml



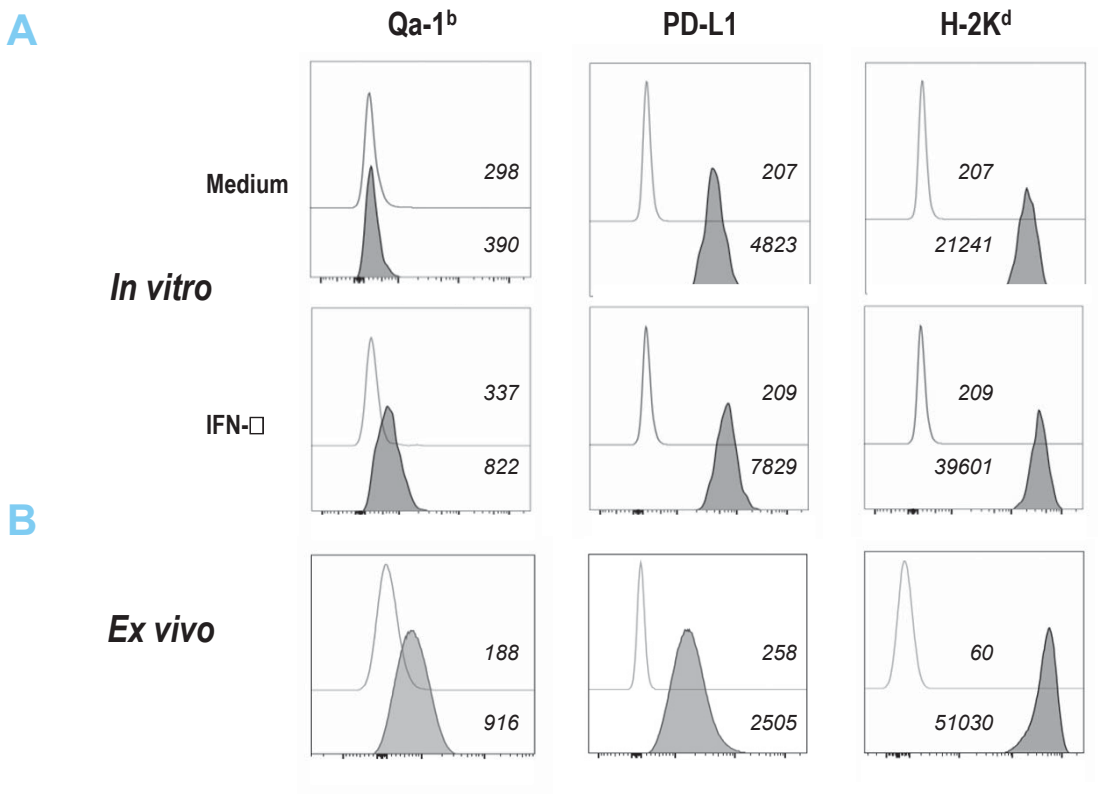


MONALIZUMAB TARGETS NKG2A CHECKPOINT ON NK CELLS AND CD8 T CELLS

- NKG2A recognize HLA-E in humans and Qa-1 in mice



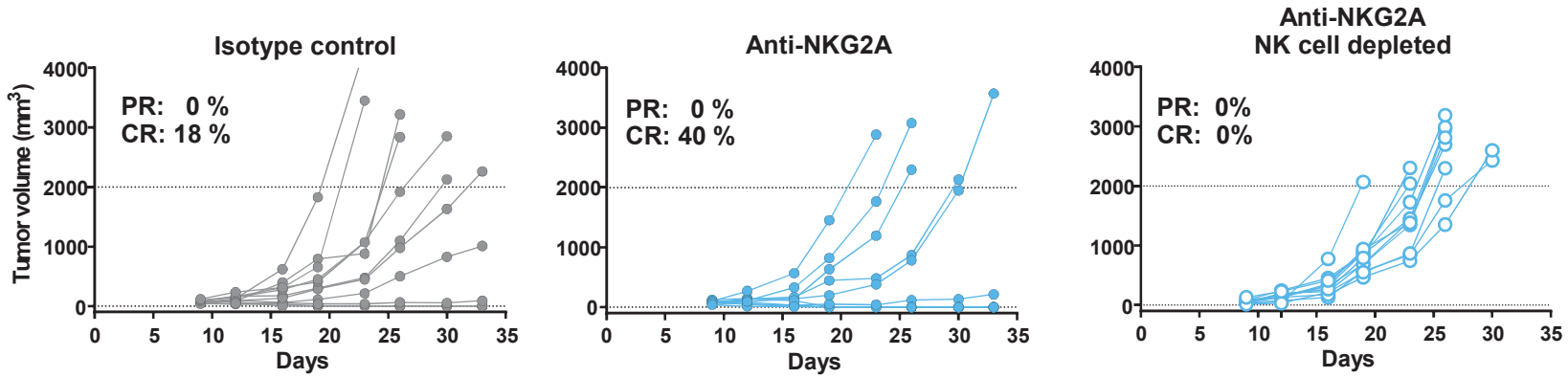
QA-1^b IS INDUCED ON A20 CELLS *IN VITRO* BY IFN-□AND *IN VIVO* AFTER ENGRAFTMENT IN MICE



Qa1 and PD-L1 expression also upregulated on tumor-infiltrating macrophages and monocytes

Sola et al., AACR 2016 poster

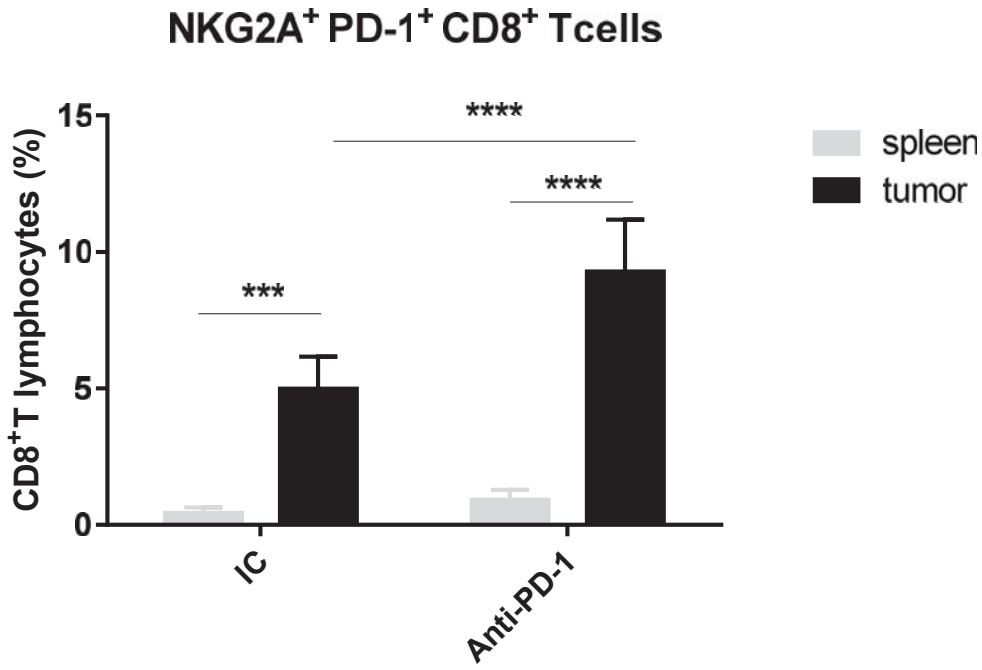
ANTI-NKG2A:
SINGLE-AGENT *IN VIVO* EFFICACY, DEPENDENT ON PRESENCE OF NK CELLS



Anti-NKG2A mAb treatment induced NK cell-mediated anti-tumor efficacy in a prophylactic setting. Mice were randomized when tumor volumes ≈ 70 mm^3 (n=10-11/group) and treated 4 times (once a week) with IC, anti-NKG2A (200 µg, iv), or anti-asialo-GM1 (100 µL, ip) mAbs. Tumor volume was measured twice a week. Individual tumor volumes of one experiment.

Sola et al., AACR 2016 poster

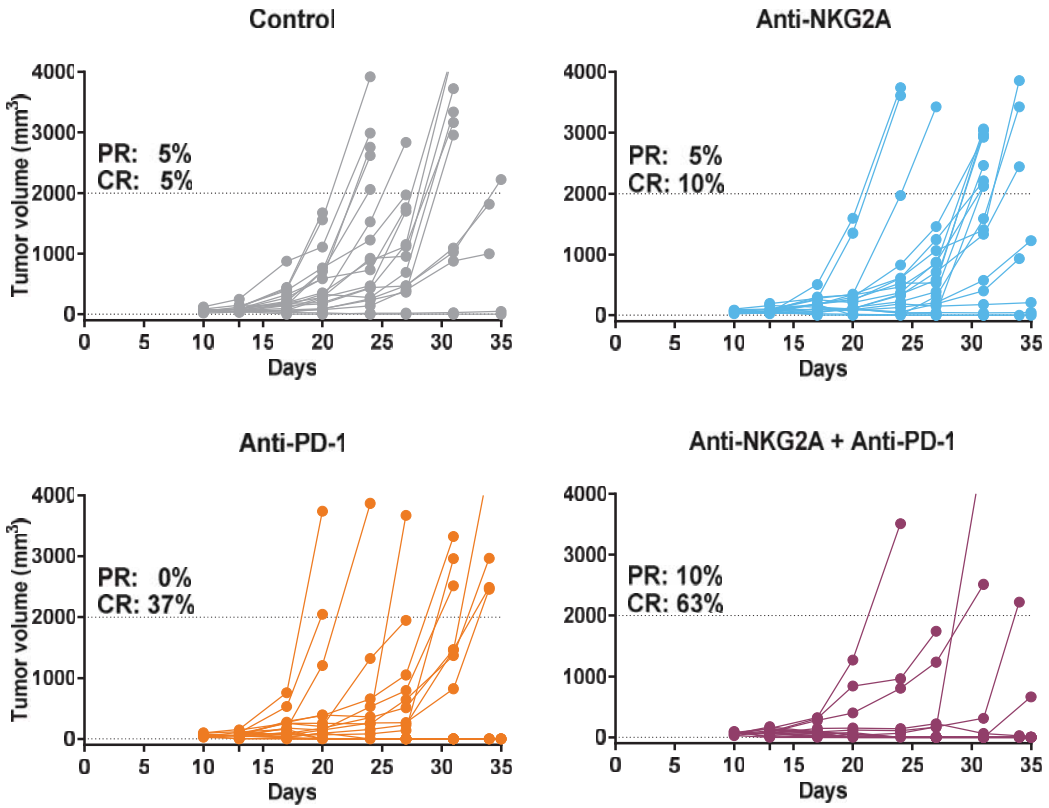
INCREASED FREQUENCY OF NKG2A$^+$ CD8 T CELLS IN MICE RESISTANT TO PD-1 PATHWAY BLOCKADE



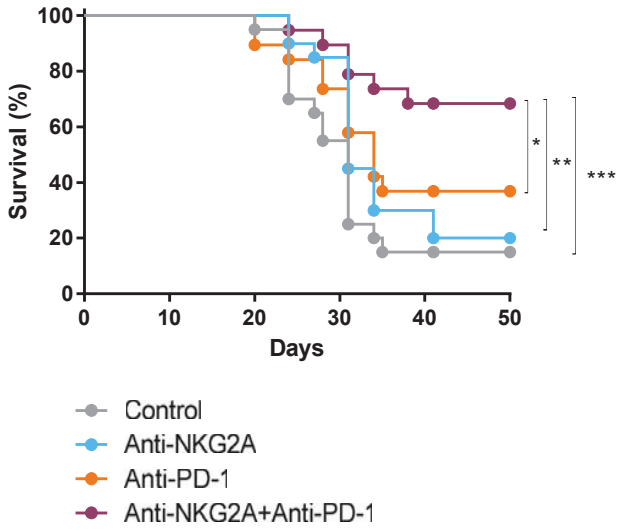
Mice treated with indicated mAbs (200 µg, ip, 3 times every 3-4 days) were sacrificed on days 21 or 28 after tumor engraftment. CD8$^+$T cells were characterized by flow cytometry. Means +/- SD of % NKG2A$^+$ PD-1$^+$ CD8$^+$ among CD8$^+$T cells. P<0.005 (***), P<0.0005 (****). N=3-6. % NKG2A$^+$ NK cells among NK cells were not modified by anti-PD-1 treatment (data not shown).

COMBINED NKG2A AND PD-1 BLOCKADE INCREASES COMPLETE RESPONSE RATE AND SURVIVAL IN MICE

A



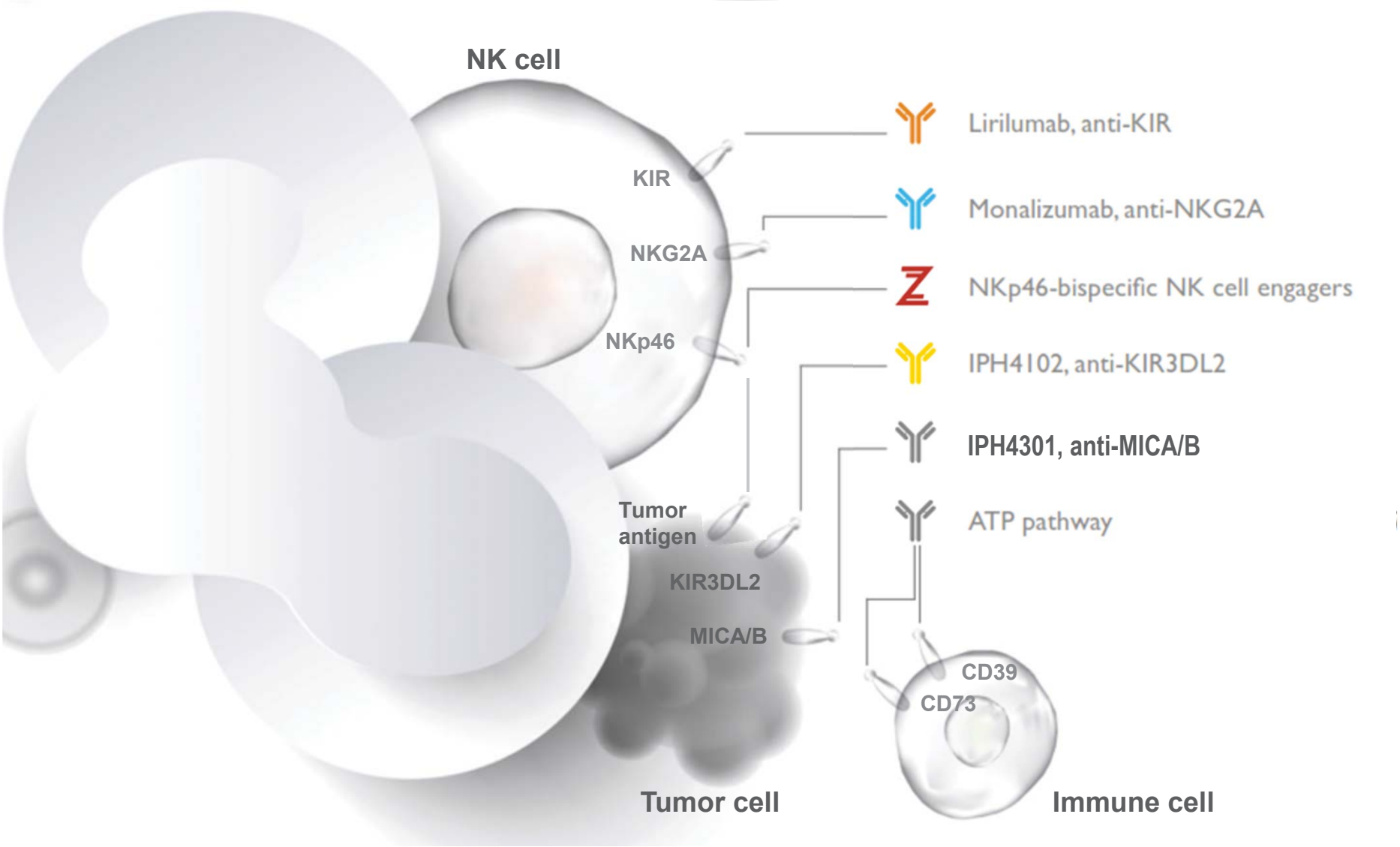
B



Mice were randomized when tumor volumes ≈ 70 mm^3 (n=19-20 mice/group) and treated 3 times (every 3-4 days) with IC, anti-NKG2A (200 µg, iv), anti-PD-1 (200 µg, ip) or anti-NKG2A and anti-PD-1 mAb. **A:** Pool of individual tumor volumes of two independent experiments. **B:** Kaplan-Meier survival. Log Rank test, P<0.05 (*), P<0.005 (**), P<0.0005 (***).

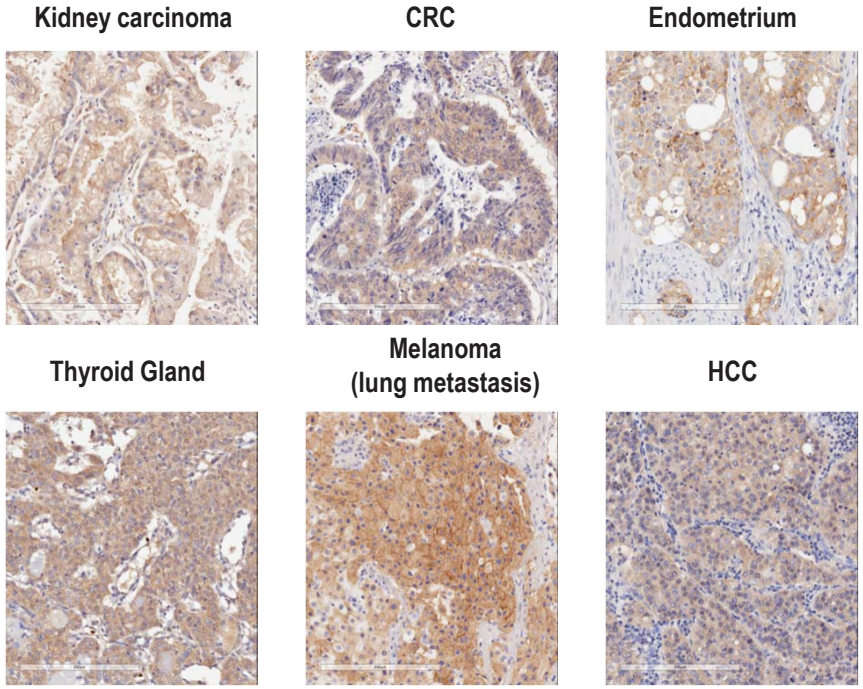
Sola et al., AACR 2016 poster

IPH4301, ANTI-MICA/B



IPH4301 IS A FIRST-IN-CLASS ANTI-MICA/B MAB

- MICA and MICB are polymorphic molecules often expressed on transformed and stressed cells
- MICA/B are ligands for NKG2D receptors on NK cells and CD8+ T cells.



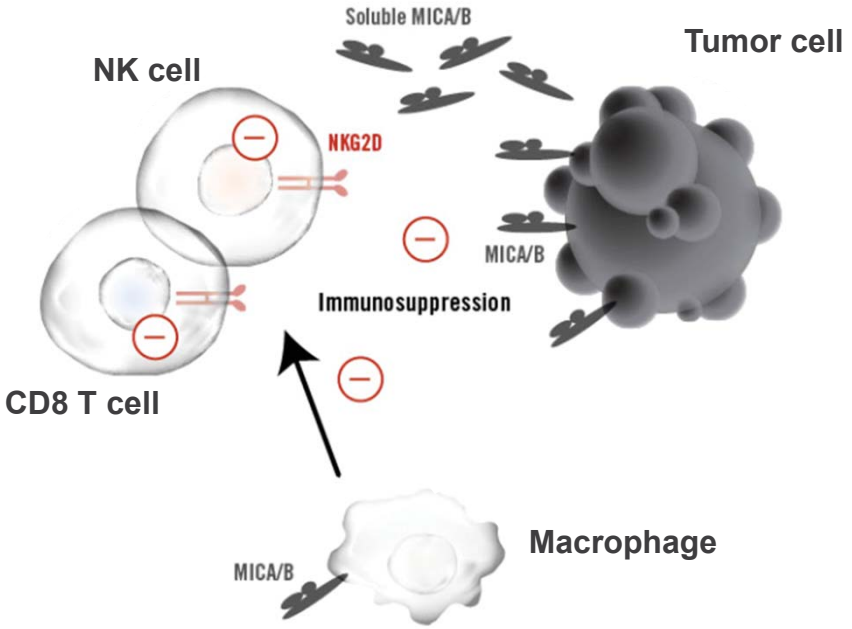
Tumor localization	Positive Cases (n=)
Kidney	100% (20)
Large intestine/Sigmoid colon	100% (20)
Endometrium	100% (10)
Thyroid Gland	100% (10)
Metastatic melanoma	90% (10)
Liver	85% (20)
Breast (TMA)	82% (28)
Melanoma	71% (7)
Lung (TMA)	62% (29)

- Chronic exposure to MICA/B down-regulates NKG2D receptors
- MICA/B can also be expressed on immunosuppressive macrophages

Morel et al., AACR 2016 poster

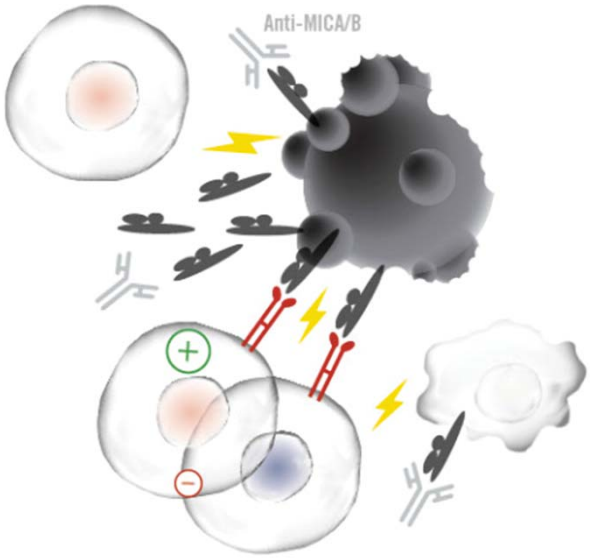
IPH4301: HUMANIZED ANTI-MICA/B

DUAL MECHANISM OF ACTION



NK and T cell inhibition by chronic exposure to MICA/B

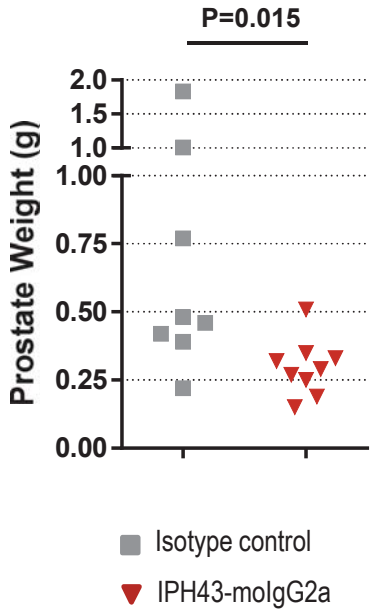
+



Dual mechanism of action: tumor antigen targeting and immunomodulation

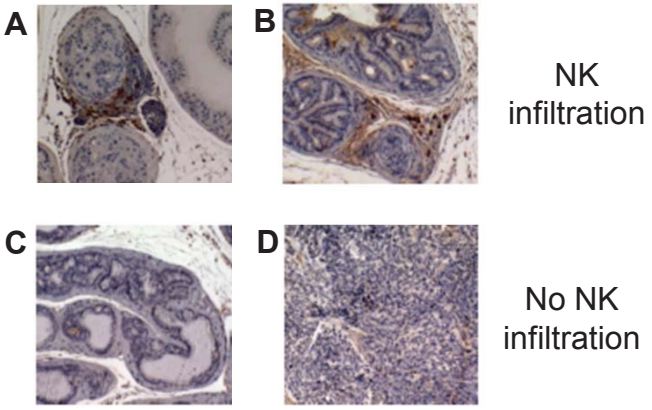
IPH4301
IN VIVO EFFICACY IN SPONTANEOUS MOUSE TUMOR MODEL

Efficacy in mouse model of prostate cancer (TRAMP/MICB)



IPH43-moIgG2a cures TRAMP-MICB mice from prostate cancer by restoring histology of prostate gland and inducing NK cell infiltration

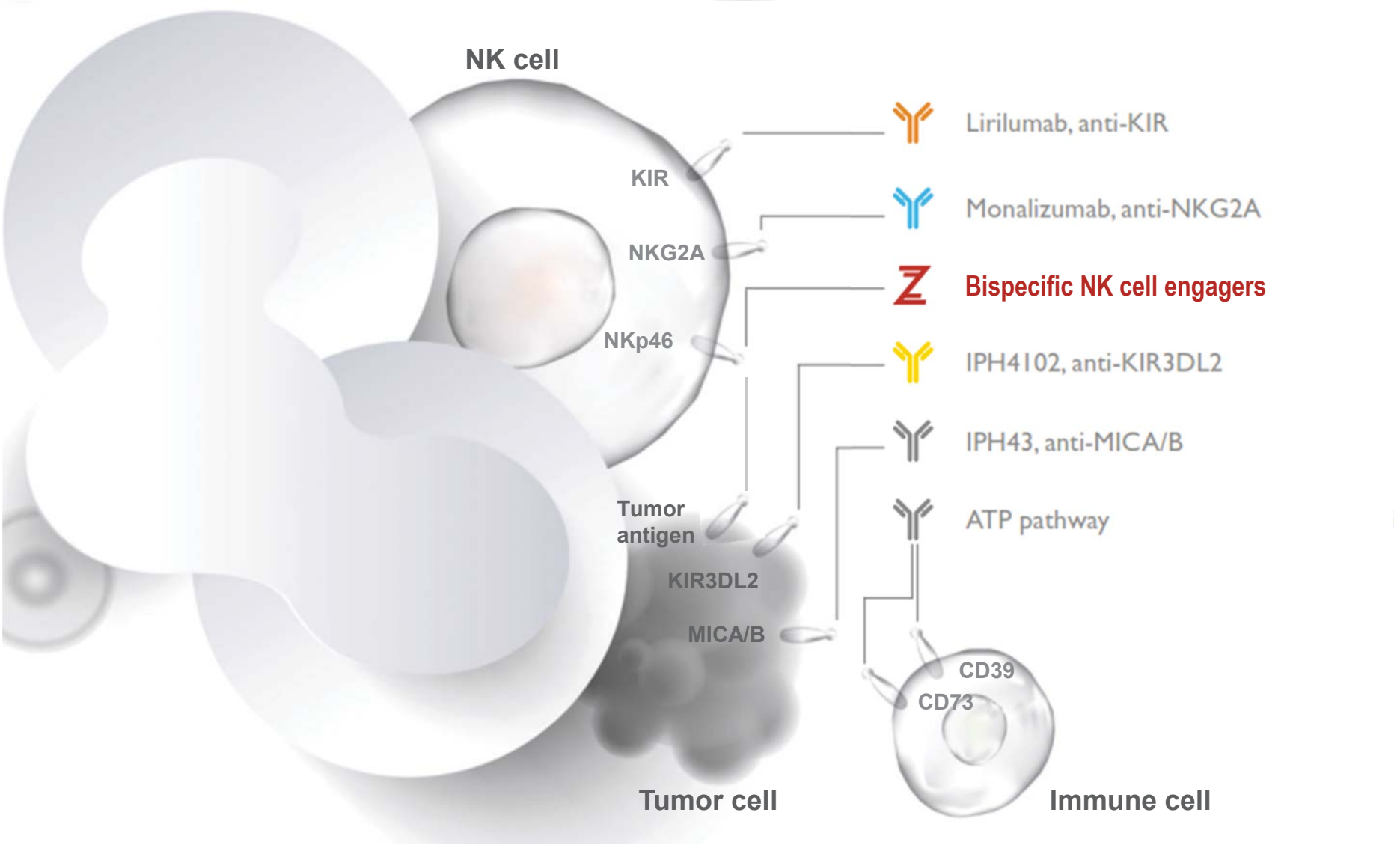
	Control	IPH43-moIG2A
Normal / Cured	0/8	4/9 (A)
Well differentiated	5/8 (C)	5/9 (B)
Poorly differentiated	3/8	0/9 (D)



IPH43-moIgG2a is mousified IPH4301

Morel et al., AACR 2016 poster

BISPECIFIC NK CELL ENGAGERS



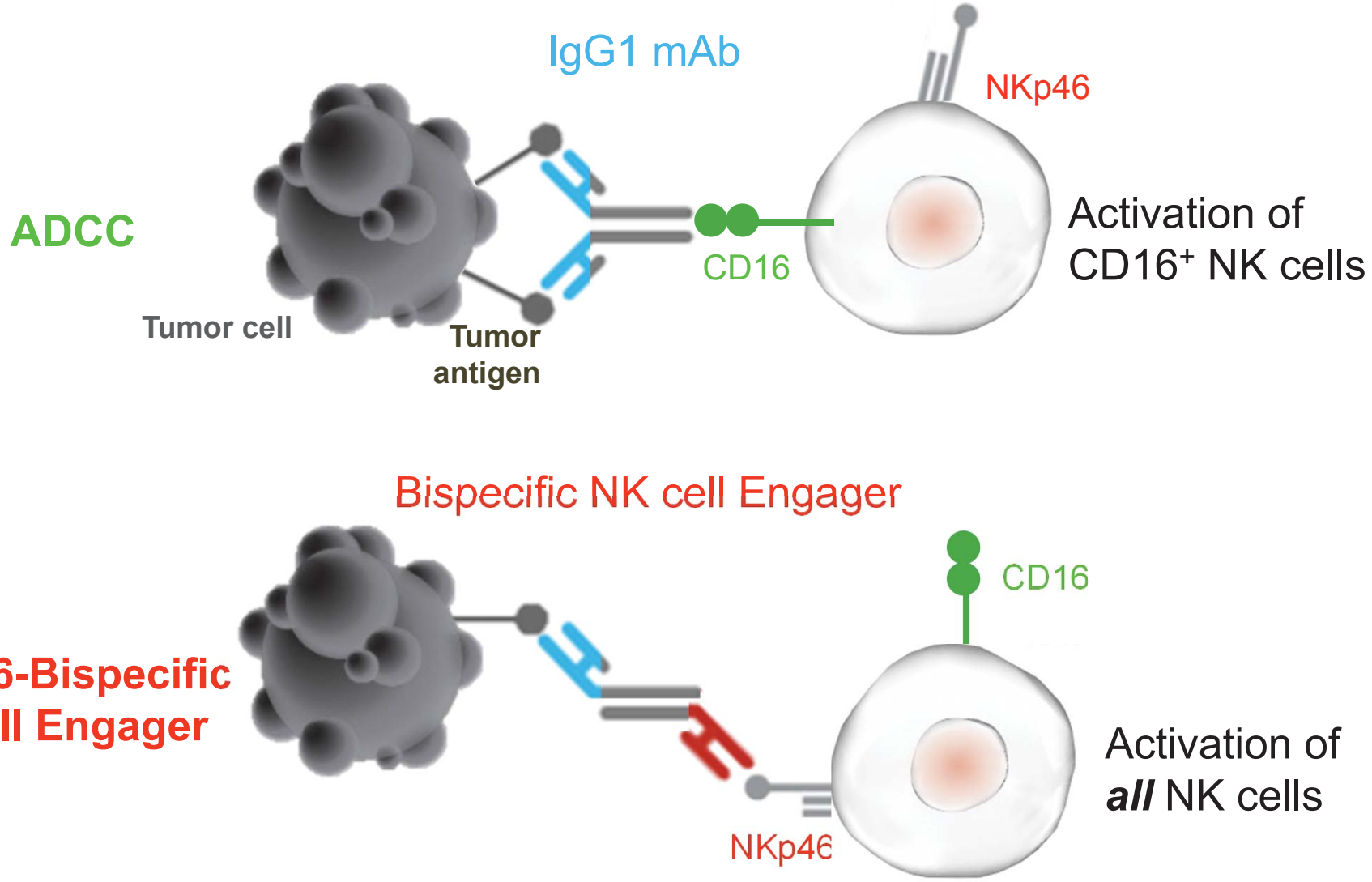
INNATE'S BISPECIFIC NK CELL ENGAGERS
TWO MAJOR INNOVATIONS

- **Stimulates NK cells instead of T cells**
  - > Innate has identified novel first-in-class agonist anti-NKp46 mAbs that trigger NK cells specifically
  - > NK cell activation has not led to cytokine storms
  - > Expect improved benefit-risk profile ⟶ attractive for development in solid tumors

- **New molecular design**
  - > Expect to solves PK and CMC issues of other formats in development
  - > Versatile platform based on modular format
  - > Patented formats

INNATE'S BISPECIFIC NK ENGAGER PLATFORM

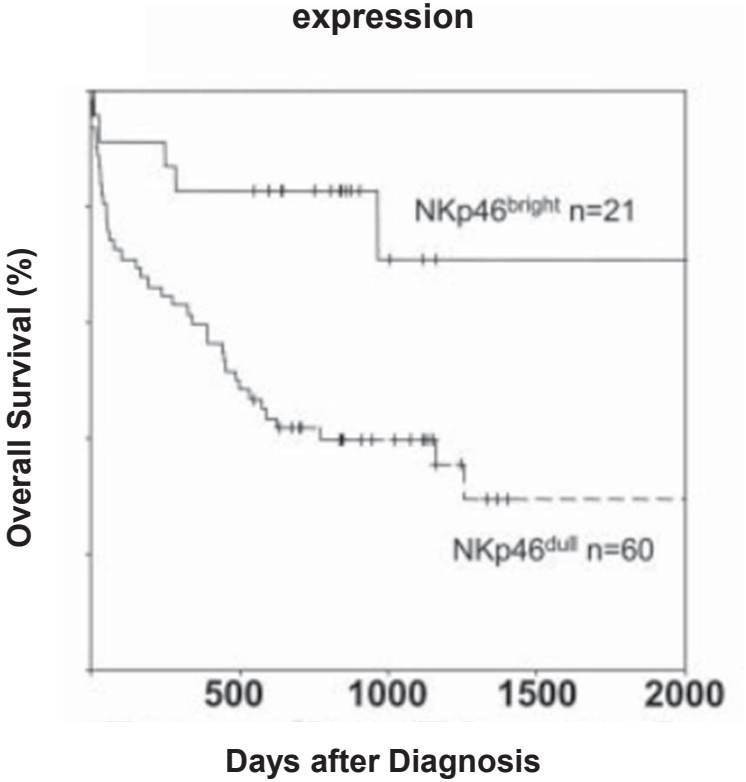
TRIGGERING NK KILLING THROUGH NKp46



WHY CHOOSE NKp46 FOR TRIGGERING NK CELLS?

- Infusion of NK cells has not resulted in cytokine storms in patients with hematological or solid tumors
- NKp46 is a potent activation receptor on NK cells
- NKp46 expression level can correlate with cancer patient survival, eg in AML
- NKp46 is expressed on all NK cells and a sub-population of NK-like ILC3 cells
- NKp46-Bispecific will specifically recruit all NK cells, and not only CD16+ NK cells

OS in AML correlates with NKp46 expression



Adapted from Fauriat et al, Blood, 2007

WHY TARGET NKP46 INSTEAD OF CD16?

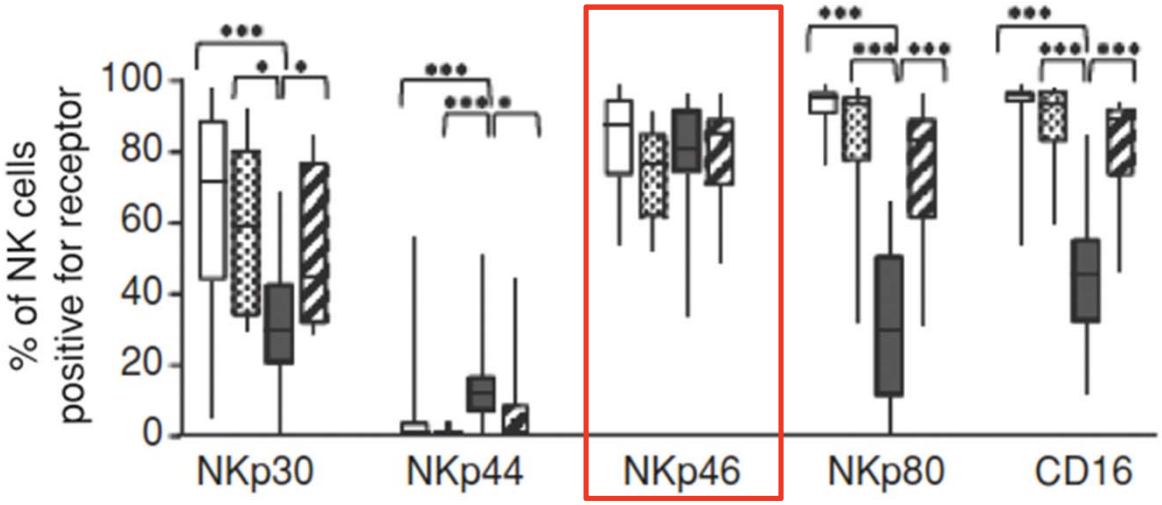
TUMOR-INFILTRATING NK CELLS OFTEN DOWNREGULATE CD16, BUT RETAIN NKp46

Microenvironment and Immunology

Cancer Research

Profound Coordinated Alterations of Intratumoral NK Cell Phenotype and Function in Lung Carcinoma

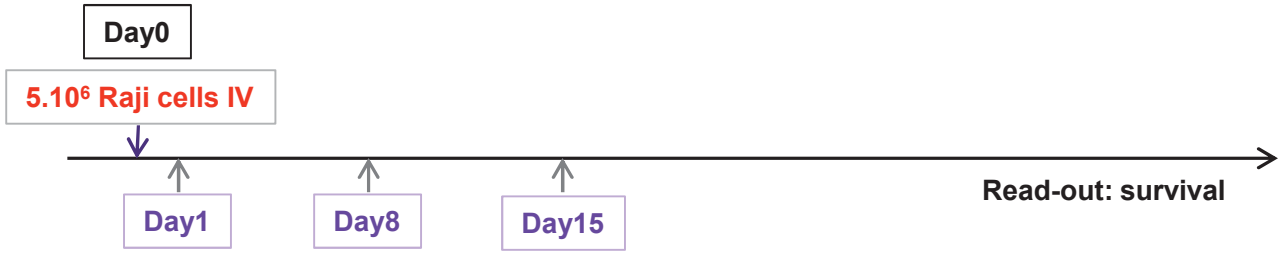
Sophia Platonova[1,2,3], Julien Cherfils-Vicini[1,2,3], Diane Damotte[1,2,3,4], Lucile Crozet[1,2,3], Vincent Vieillard[5], Pierre Validire[1,2,3,6], Pascale André[8], Marie-Caroline Dieu-Nosjean[1,2,3], Marco Alifano[4], Jean-François Régnard[3,4], Wolf-Herman Fridman[1,2,3,7], Catherine Sautès-Fridman[1,2,3], and Isabelle Cremer[1,2,3]



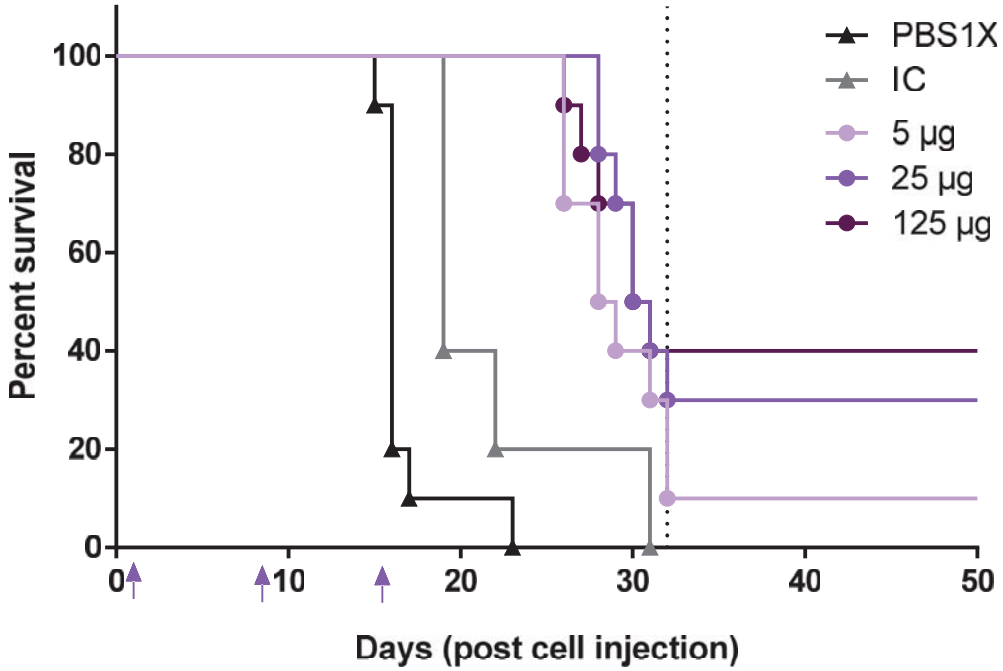
- Healthy donors blood (n=30)
- Patients blood (n=10)
- Intratumoral (n=30)
- Nontumoral distant lung (n=10)

Lung Carcinoma : Platonova et al, Cancer Research 2011
Breast Cancer : Mamessier et al, J Clin Invest. 2011

NKP46-CD19 SURROGATE PROMOTE TUMOR KILLING *IN VIVO*



Survival of CB17 SCID mice IV engrafted with Raji cells (5 M) treated with Anti-CD19 NK cell engager

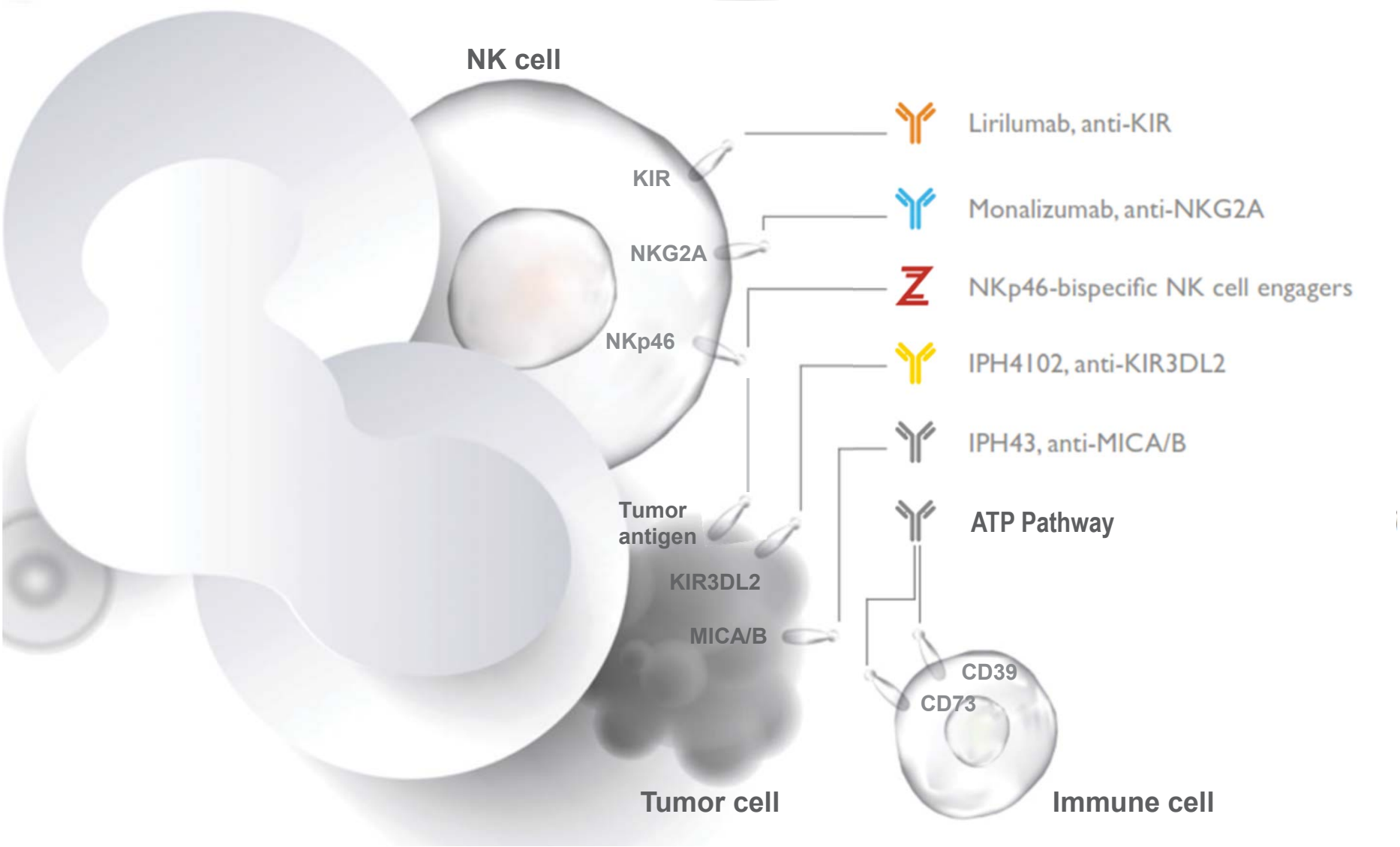


PROPRIETARY NKP46 BISPECIFIC PLATFORM

- Stimulates NK cells instead of T cells
  - > Attractive for development in solid cancer indications, including non-inflamed
- Novel molecular design
  - > Patented design, versatile modular format
- We are bulding a pipeline of proprietary bi-specific product candidates
- Non-exclusive NKp46 technology partnerships, like recent agreement with Sanofi

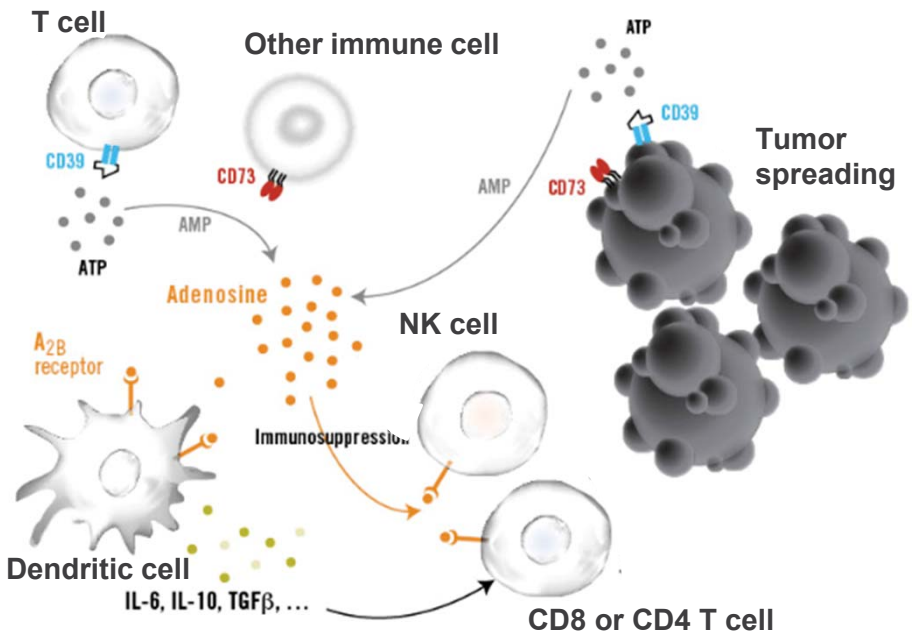
ADENOSINE PATHWAY

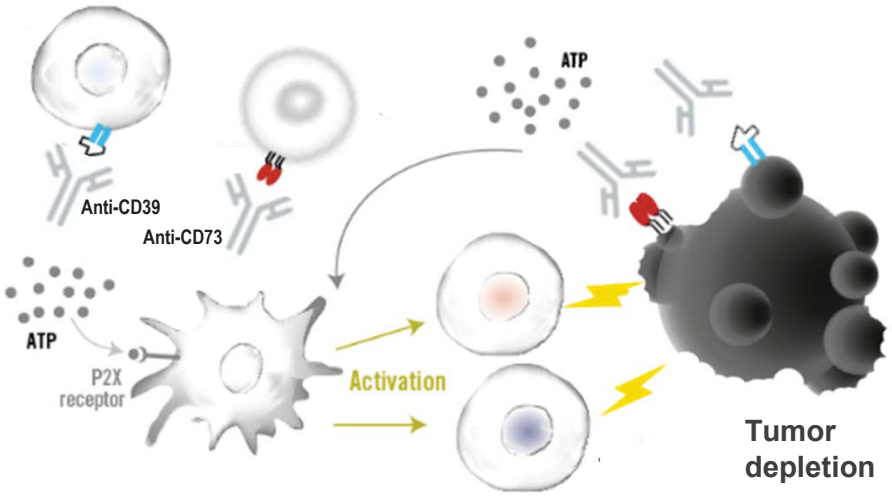
TARGETING IMMUNOSUPPRESSIVE TUMOR MICROENVIRONMENT



ADENOSINE PATHWAY: ANTI-CD39 & ANTI-CD73

TARGETING IMMUNOSUPPRESSIVE TUMOR MICROENVIRONMENT





ATP : adenosine triphosphate **AMP :** adenosine monophosphate

- CD39 and CD73 are enzymes expressed on regulatory T cells, immune cells and tumor cells in the tumor microenvironment
  - > Promote immunosuppression by degrading pro-inflammatory ATP into immunosuppressive adenosine
  - > Blocking this pathway may stimulate anti-tumor immunity across a wide range of tumors

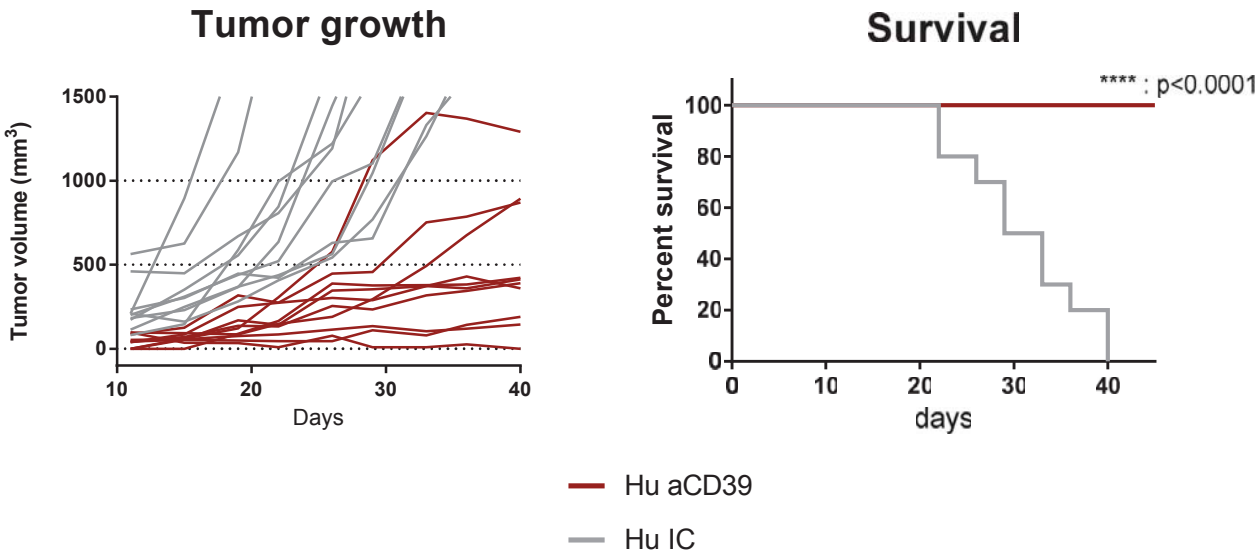
CD39:* Augier et al. *AACR 2016 poster*; *CD73*: Giraudon-Paoli et al., *AACR 2016 poster

IPH52

FIRST IN CLASS ANTI-CD39 ANTIBODY

- IPH52 displays single agent activity

Humanized mAb inhibits tumor growth in xenogeneic tumor model



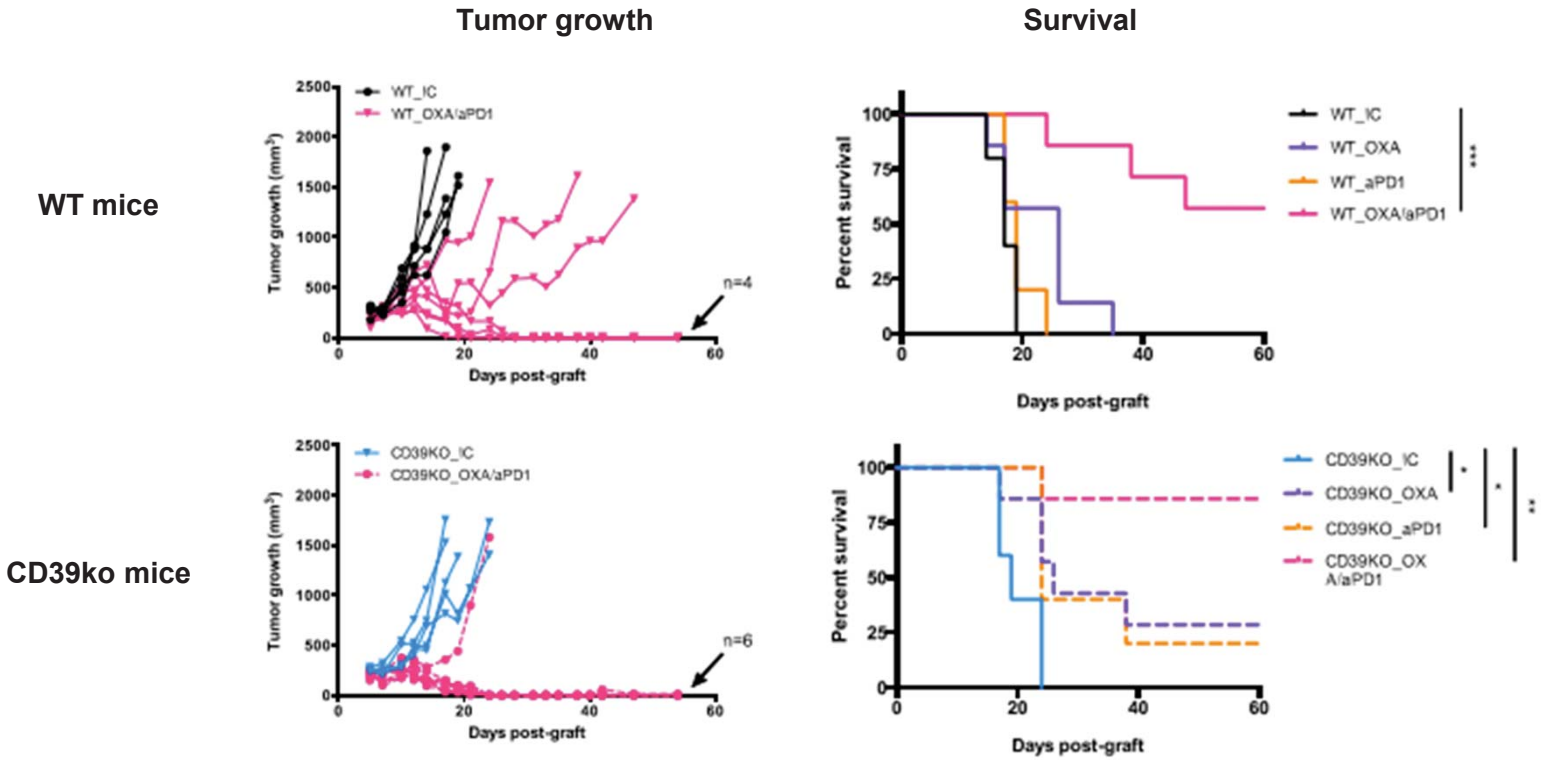
Augier et al., AACR 2016 poster

IPH52

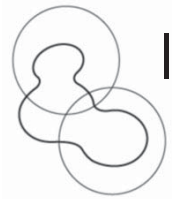
POTENTIAL FOR COMBINATION WITH CANCER TREATMENTS

- CD39 disruption drives antitumor immune responses, either alone or in combination with PD-1 checkpoint blockers, ADCC antibodies and immunogenic chemotherapy, suggesting broad development potential

Treatment with anti-PD1 and oxaliplatin in CD39 KO mice leads to 86% CR



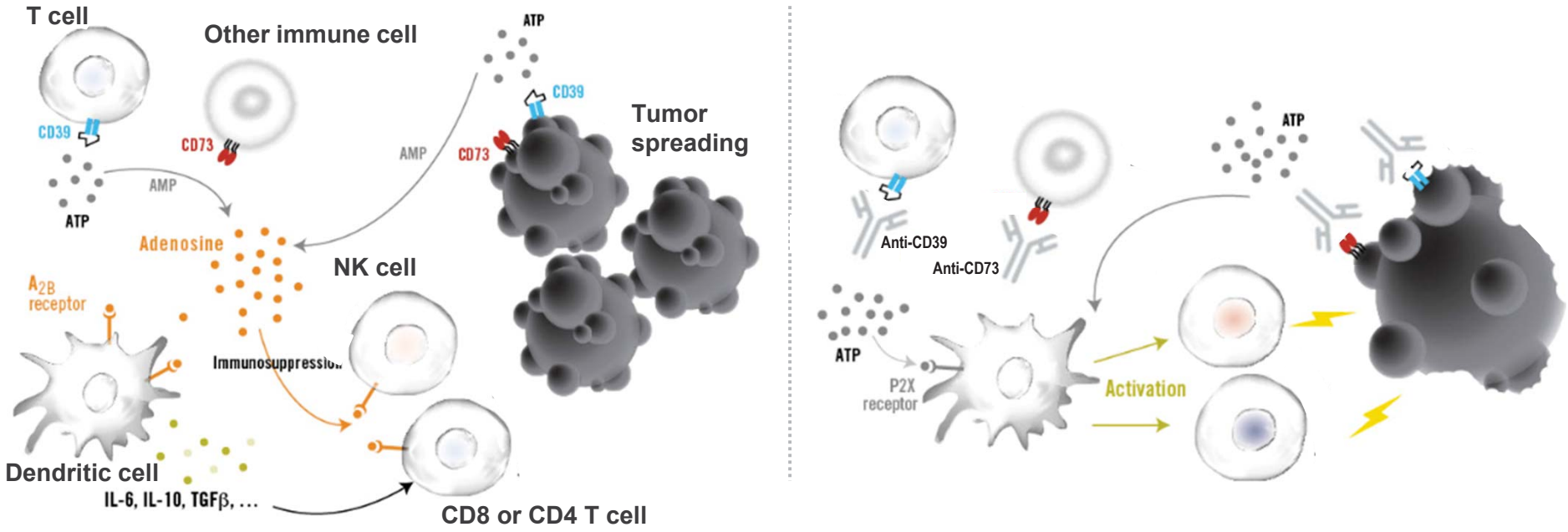
Lapierre et al., AACR 2016 poster (OREGA Biotech)



IPH52 (ANTI-CD39)

- First-in-class humanized anti-CD39 mAb with high affinity and specificity for CD39 blocks ATPase activity *in vitro,* both on tumor cells and immune cells
- *In vivo*, humanized anti-CD39 mAb significantly inhibits CD39/CD73 positive tumor growth
- Broad development potential suggested by experiments in CD39 knock-out mice, including combination therapy with chemotherapy, ADCC-antibodies and/or immune checkpoint inhibitors
- IPH52 is currently in lead optimization

ANTI-CD73: NEW CHECKPOINT INHIBITOR PROGRAM TARGETING THE TUMOR MICROENVIRONMENT



- Targeting CD73 may block tumor cell metastasis by reducing the generation of immunosuppressive adenosine
- A panel of antibodies were discovered that inhibit CD73 function by different mechanisms; the most interesting were humanized

ATP : adenosine triphosphate **AMP :** adenosine monophosphate

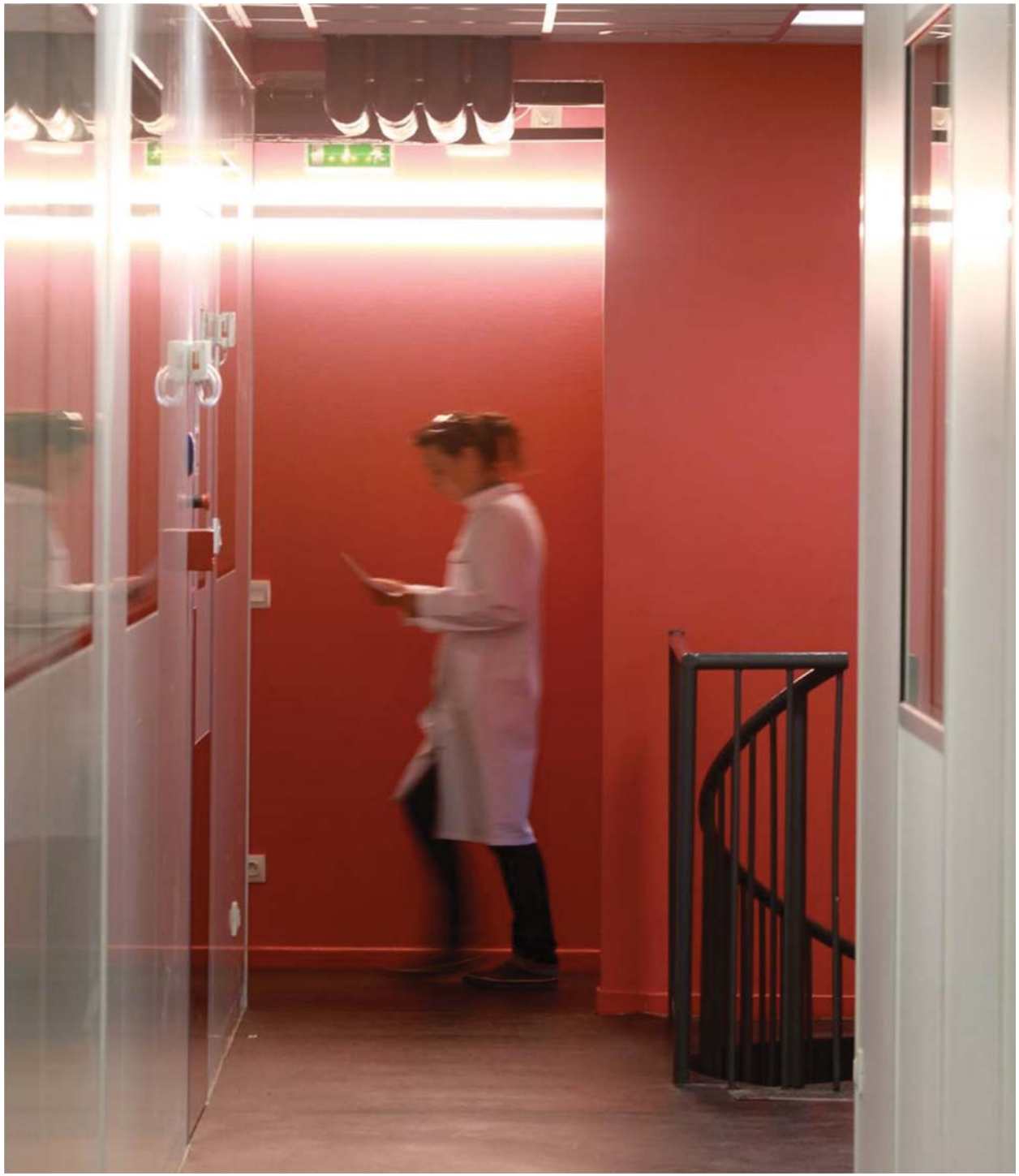
INNATE PHARMA'S R&D STRATEGY AND APPROACHES IN IMMUNO-ONCOLOGY

First-in-class checkpoint antibodies targeting NK cell receptors

Novel anti-NKp46 bispecific platform technology:
Directing NK cells to kill tumors

Targeting immuno-suppression in tumor microenvironment to unleash cytotoxic NK and T cells

A differentiated approach based on NK cells



ONGOING CLINICAL PROGRAMS

LIRILUMAB

FIRST-IN-CLASS ANTI-KIR MAB

LICENSED TO BRISTOL-MYERS SQUIBB

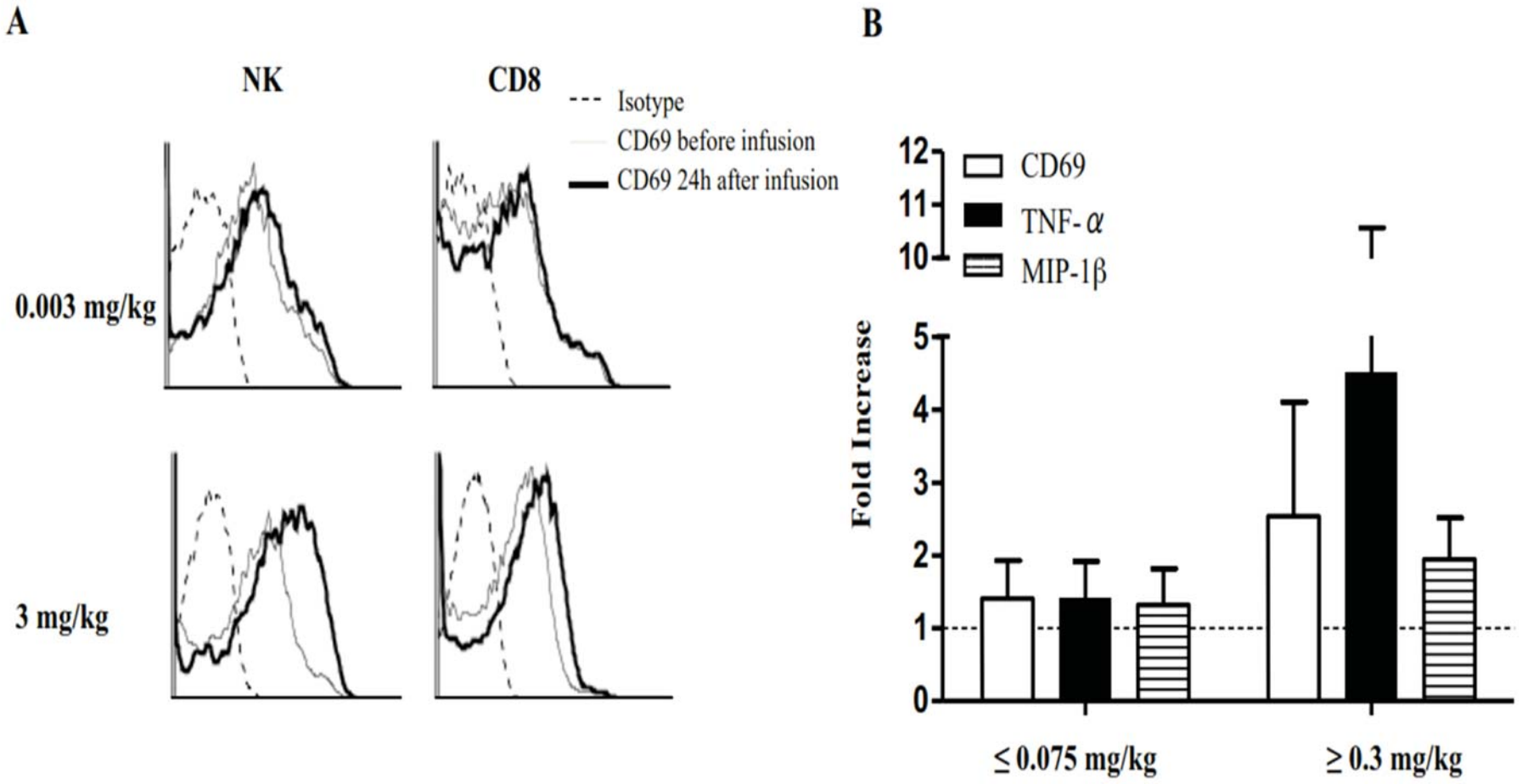
PHASE I TRIAL WITH HYBRIDOMA ANTI-KIR (IPH2101)

- Elderly AML patients in complete remission after induction and consolidation treatment - maintenance setting
- Phase I dose-escalation including 23 patients in first CR, and study extension including 12 additional patients in CR - Doses ranged from 0.0003 to 3 mg/kg – Full KIR saturation at doses ≥1mg/kg
- Good tolerance with mild and transient adverse events. Maximum tolerated dose (MTD) not reached. Clear PK/PD relationship

Vey et al., Blood 2012 and ASH 2013 poster

PHASE I TRIAL WITH HYBRIDOMA ANTI-KIR (IPH2101)

INDUCTION OF NK CELL ACTIVATION MARKERS



Vey et al., Blood, 2012

PHASE I TRIAL WITH HYBRIDOMA ANTI-KIR (IPH2101)

TRENDS IN CLINICAL OUTCOME RELATED TO KIR OCCUPANCY

- Suggested a correlation between full receptor occupancy and efficacy

- Clinical outcome (OS & PFS*) compared favorably to reports in comparable patient population

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

* OS: Overall Survival, PFS: Progression Free Survival

**OS and PFS analyzed on 32 pts: 2 patients from extension excluded, one in CR2 and one for early relapse within 5-days and one in escalating part for absence of treatment)

Vey et al., Blood 2012 and ASH 2013 poster

LIRILUMAB PHASE I

- 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 tumor 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)
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%)**

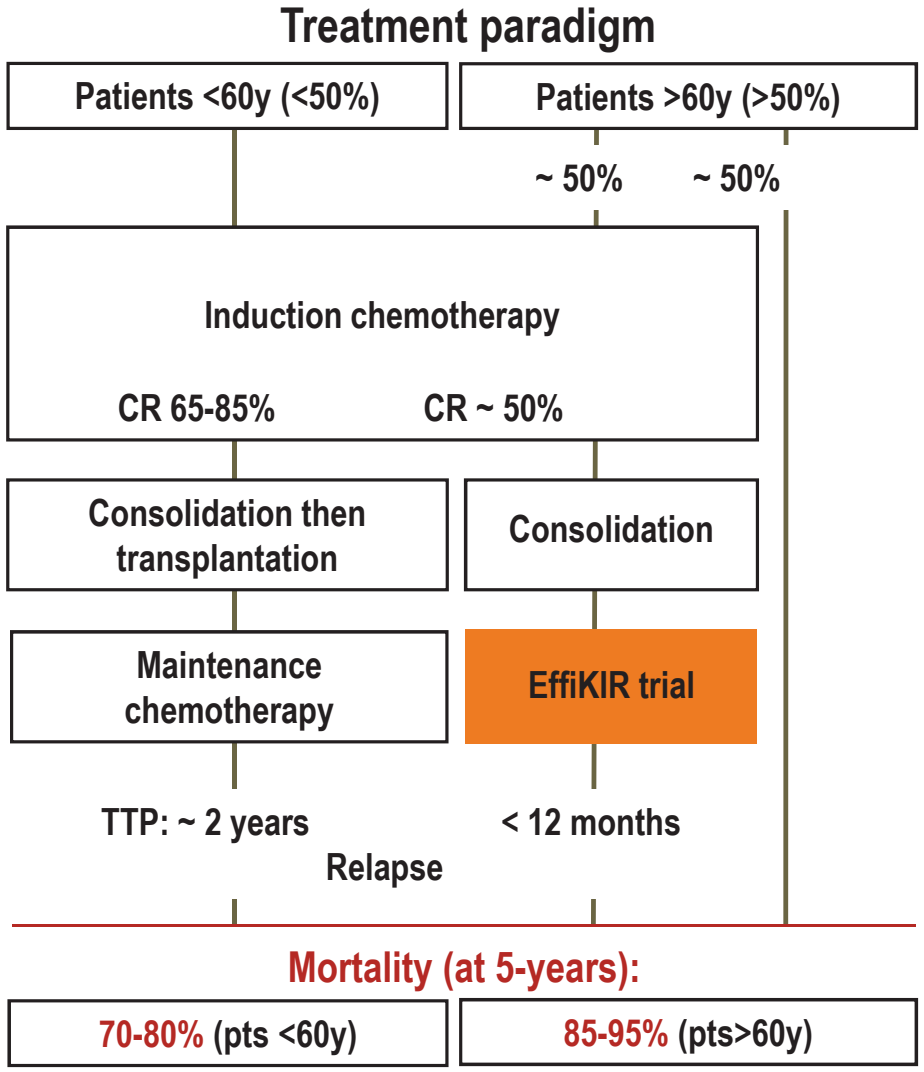
* 7 (18.9%) = Disease progression

Vey et al., ASCO 2015 poster

EFFIKIR POSITIONING IN ACUTE MYELOID LEUKEMIA

STRONG MEDICAL NEED IN ELDERLY PATIENTS

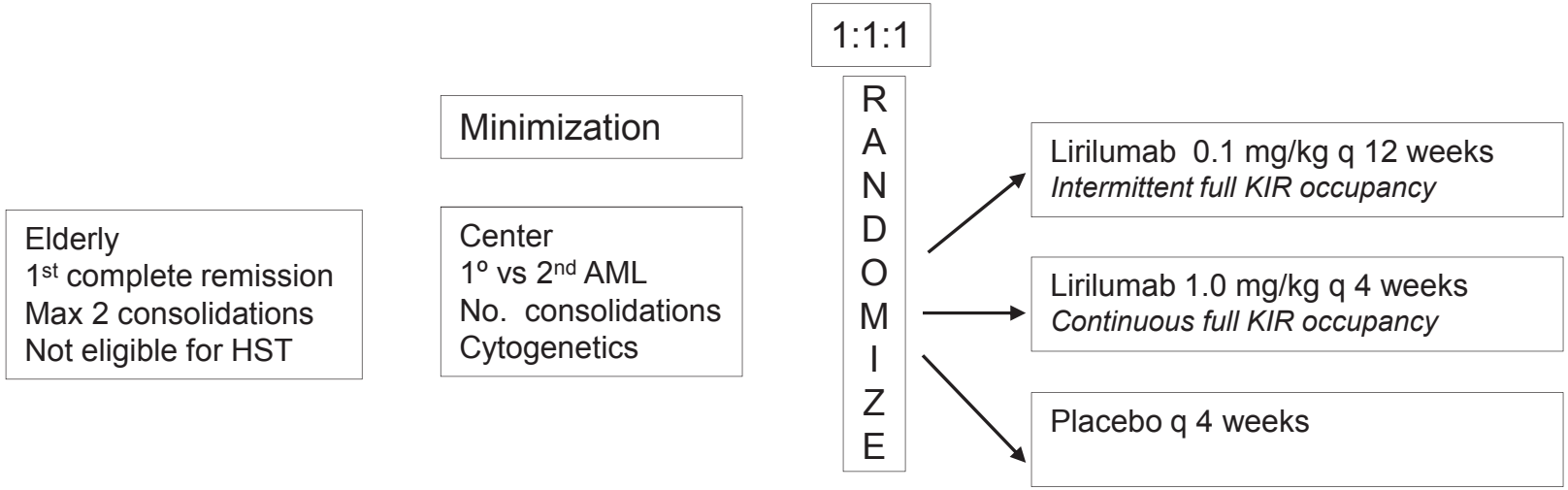
- 5-year survival rate in elderly patients with AML is 5 to 15%
- No current standard of care for elderly patients in post-induction setting
- Intensive development effort in AML focused on relapsed / refractory disease
- Lirilumab tested in maintenance for elderly patients



EFFIKIR PHASE II TRIAL

DOUBLE-BLIND PLACEBO-CONTROLLED RANDOMIZED TRIAL IN AML

- Target enrollment completed in July 2014 (150 patients)
- Data on leukemia free survival (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**

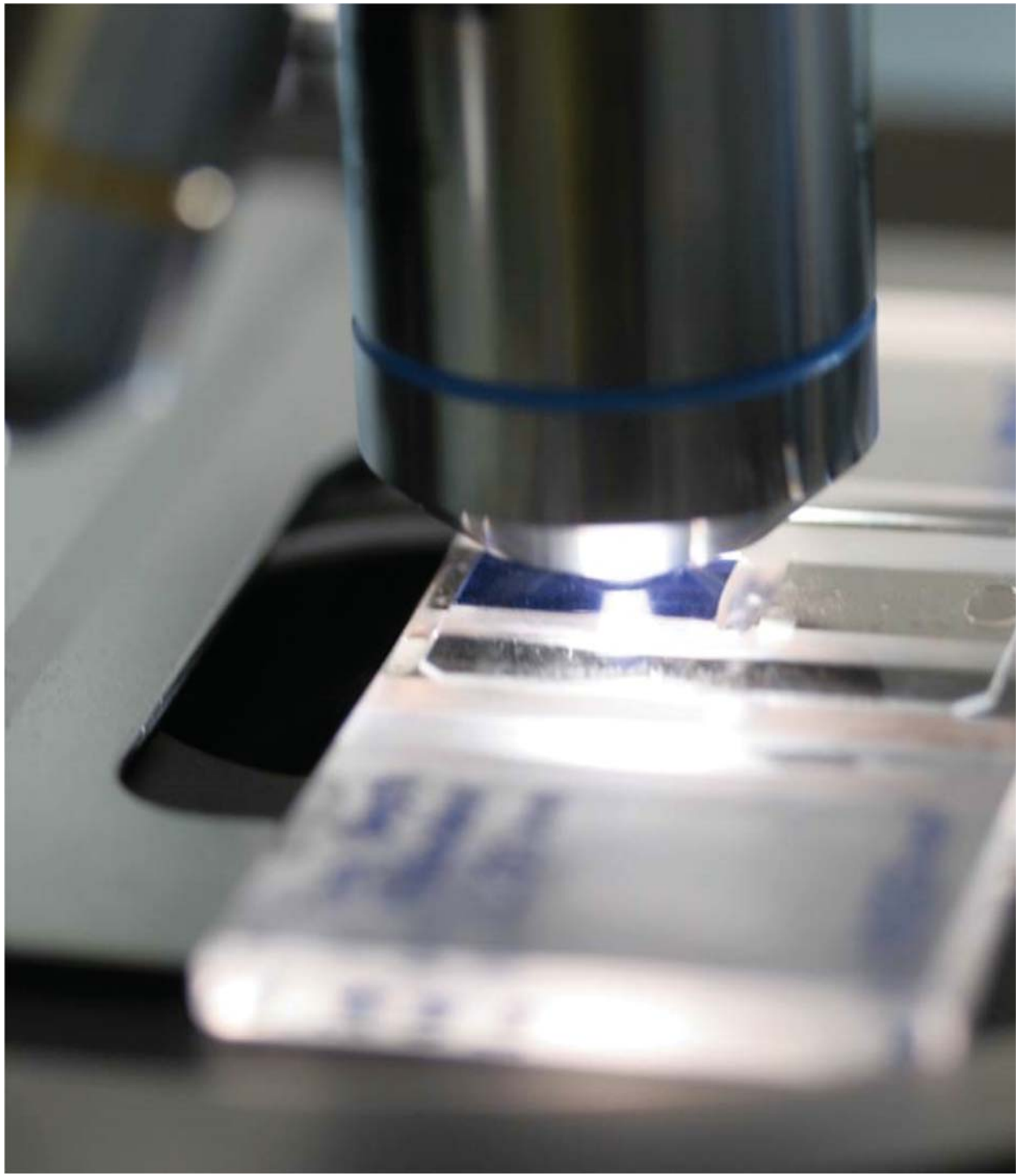
CLINICAL PROGRAMS WITH LIRILUMAB

NEAR 700 PATIENTS TO RECEIVE LIRILUMAB

		PHASE	PATIENTS	INDICATION	STATUS
EffiKIR	Monotherapy	Randomized Phase II	150	Acute Myeloid Leukemia Maintenance setting	Data on LFS expected 2H 2016
Combination	Nivolumab	Phase I with dose escalation and cohort expansion	162	Selected solid tumors: MEL, NSCLC, GI, SCCHN, HCC	Enrollment close to completion
	Nivolumab	Phase I with dose escalation	315(1)	Selected hematologic tumors: R/R NHL, HL, MM or CML	Started October 2014
	Elotuzumab	Phase I with dose escalation and 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	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 (nivolumab, nivolumab + ipilimumab, nivolumab + lirilumab) / (2) Two arms (elotuzumab + lirilumab, elotuzumab + urelumab)



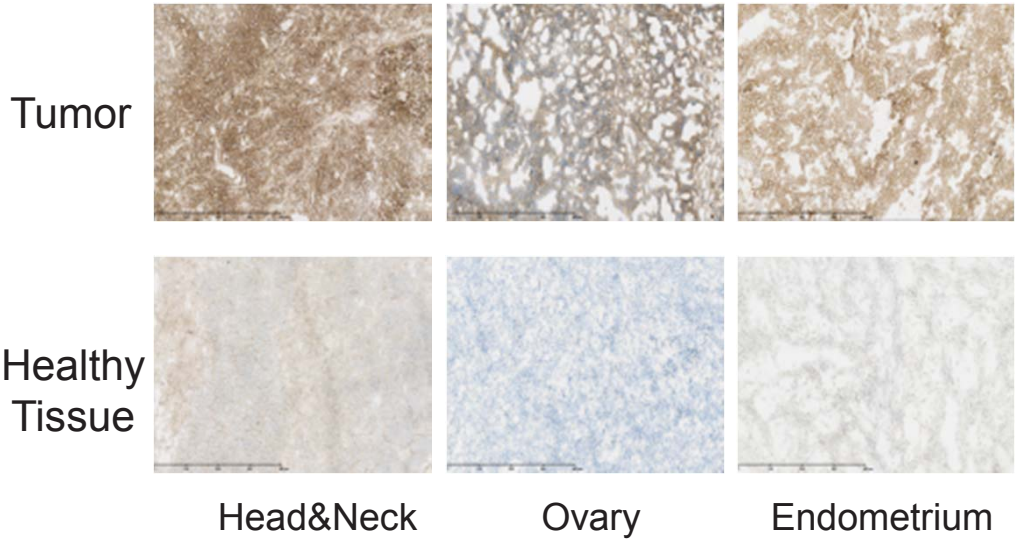
MONALIZUMAB

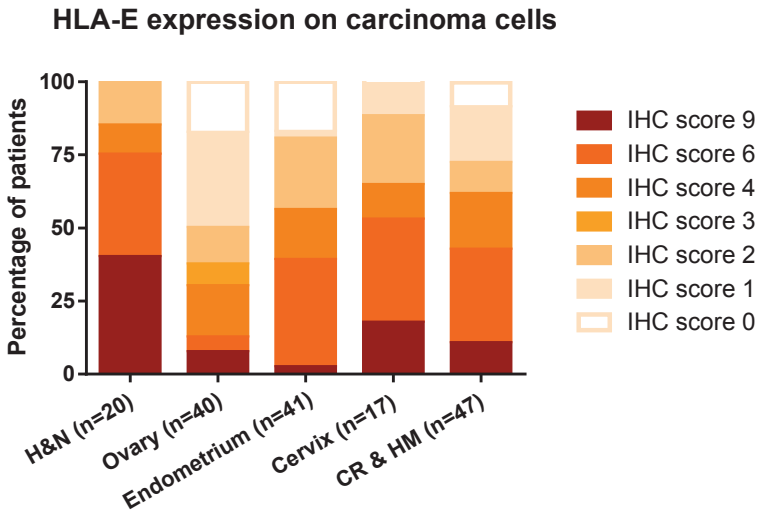
FIRST-IN-CLASS ANTI-NKG2A MAB

CO-DEVELOPMENT AND COMMERCIALIZATION AGREEMENT WITH ASTRAZENECA

MANY TUMORS OVEREXPRESS HLA-E, THE LIGAND OF NKG2A

- HLA-E upregulated on a wide variety of tumor types:
  - > H&N, Ovarian, Endometrium, Colorectal, Cervix, Lung, Oesophagus, CLL
- Restricted expression on normal tissues
- Clinical development plan informed by expression of HLA-E





INITIAL CLINICAL DEVELOPMENT PLAN WITH MONALIZUMAB

CLINICAL DEVELOPMENT PLAN INFORMED BY EXPRESSION OF HLA-E

		PHASE	PATIENTS	INDICATION	STATUS	LOCALIZATION
	Monotherapy	Phase I/II	43	Head & Neck Neo-adjuvant setting	Started Dec. 2014	Europe
	Monotherapy	Phase I/II with dose escalation	Up to 98	Gynecological cancers incl. ovarian	Started Sept. 2015	Canada
Combination	Ibrutinib	Phase I/II with dose escalation and cohort expansion	Up to 45	Chronic Lymphocytic Leukemia Relapsed or refractory	Started Oct. 2015	US
	Cetuximab	Phase I/II with dose escalation and cohort expansion	Up to 70	Head & Neck Relapsed or refractory	Started Dec. 2015	US and Europe
	Durvalumab (anti-PD-L1)	Phase I with dose escalation	Up to 208	Solid tumors	Started Feb. 2016	US and Europe

IPH4102

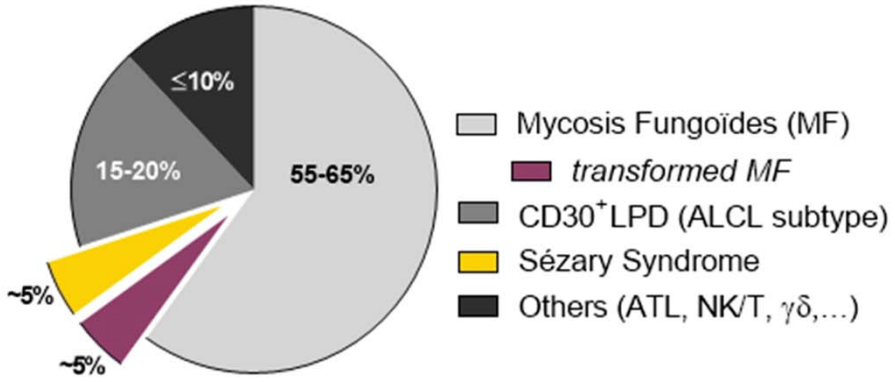
FIRST-IN-CLASS ANTI-KIR3DL2 CYTOTOXIC MAB

IN-HOUSE DEVELOPMENT

CUTANEOUS T CELL LYMPHOMA (CTCL)
ORPHAN DISEASE WITH HIGH MEDICAL NEED

- CTCL is a group of rare and heterogeneous cutaneous lymphomas of T cells with poor prognosis and few therapeutic options at advanced stages
  - > ~6,000 patients in EU and US
  - > The most common CTCL subtypes are Mycosis fungoides (MF) and Sézary syndrome (SS)
  - > 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

Relative frequency of CTCL subtypes per WHO-EORTC classification [1-5]



	5-year Overall Survival
Mycosis Fungoïdes (MF)	20 to 95%*
transformed MF	≤ 15%
CD30+LPD (ALCL subtype)	76 to 96%
Sézary Syndrome	~10%
Others (ATL, NK/T, γδ,…)	≤ 20%

* Depending on TNMB stage

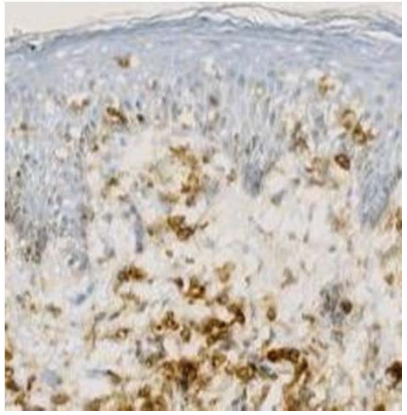
1. Agar et al., JCO 2010; 2. Kempf et al., Blood 2011; 3. Willemze, Blood 1997; 4. Willemze et al., Annals Oncol 2013; 5. Kim et al., Arch Dermatol 2003

KIR3DL2 IS SPECIFICALLY EXPRESSED ON CUTANEOUS AND CIRCULATING CTCL CELLS

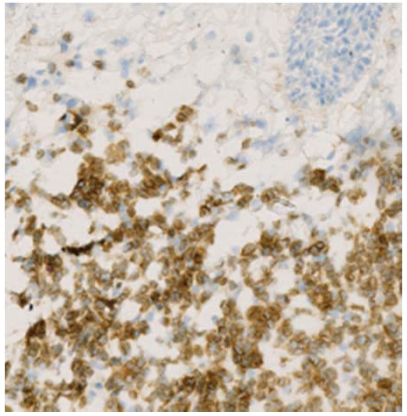
- Irrespectively of disease grade and on most subtypes
  - > ~65% of all CTCL;
  - > Expression is more prominent in Sézary syndrome, transformed mycosis fungoides and CD30+ LPD (ALCL subtype): from 80% to 100% of patients
- Restricted expression on normal tissues

Patients biopsies stained with Innate's anti-KIR3DL2 mAb

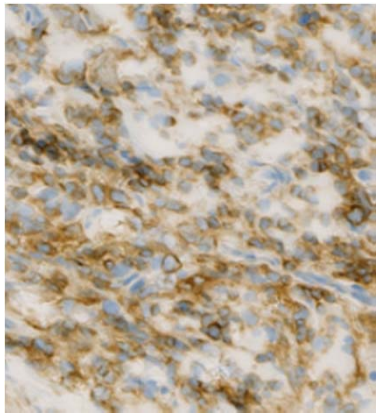
SS pt #1, grade IIIB
87% KIR3DL2$^+$ tumor cells[1]



tMF pt #1, grade IIB
96% KIR3DL2$^+$ tumor cells[2]



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



1-3. Internal data

PHASE I STUDY OF IPH4102
STARTED IN 2015

- Dose-escalation + cohort expansion study in KIR3DL2+ patients:
  - > Dose-escalation: 10 dose levels of repeated administrations of IPH4102
  - > Cohort expansion: 2 cohorts of 10 patients each in SS and tMF
    - CTCL subtypes with the most frequent KIR3DL2 expression
    - Highest unmet medical need

- EU and US, involving referral expert centers

- 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
- Sizable market opportunity within the means of Innate Pharma; strategy is to retain full development and marketing rights to IPH4102

SUMMARY

- A unique, differentiated approach based on NK cells
- Broad pipeline of first-in-class checkpoint antibodies with diverse MOAs
- Adressing heterogenous patient population with antibodies targeting distinct checkpoints and diverse NK and T cell populations
  - > Single-agent and combination therapy in broad range of cancer indications
- Approaches for different types of PD-1 refractory patients
  - > Including new proprietary bispecific platform
- First-in-class approach for targeting suppressive tumor microenvironment to unleash NK and T cells

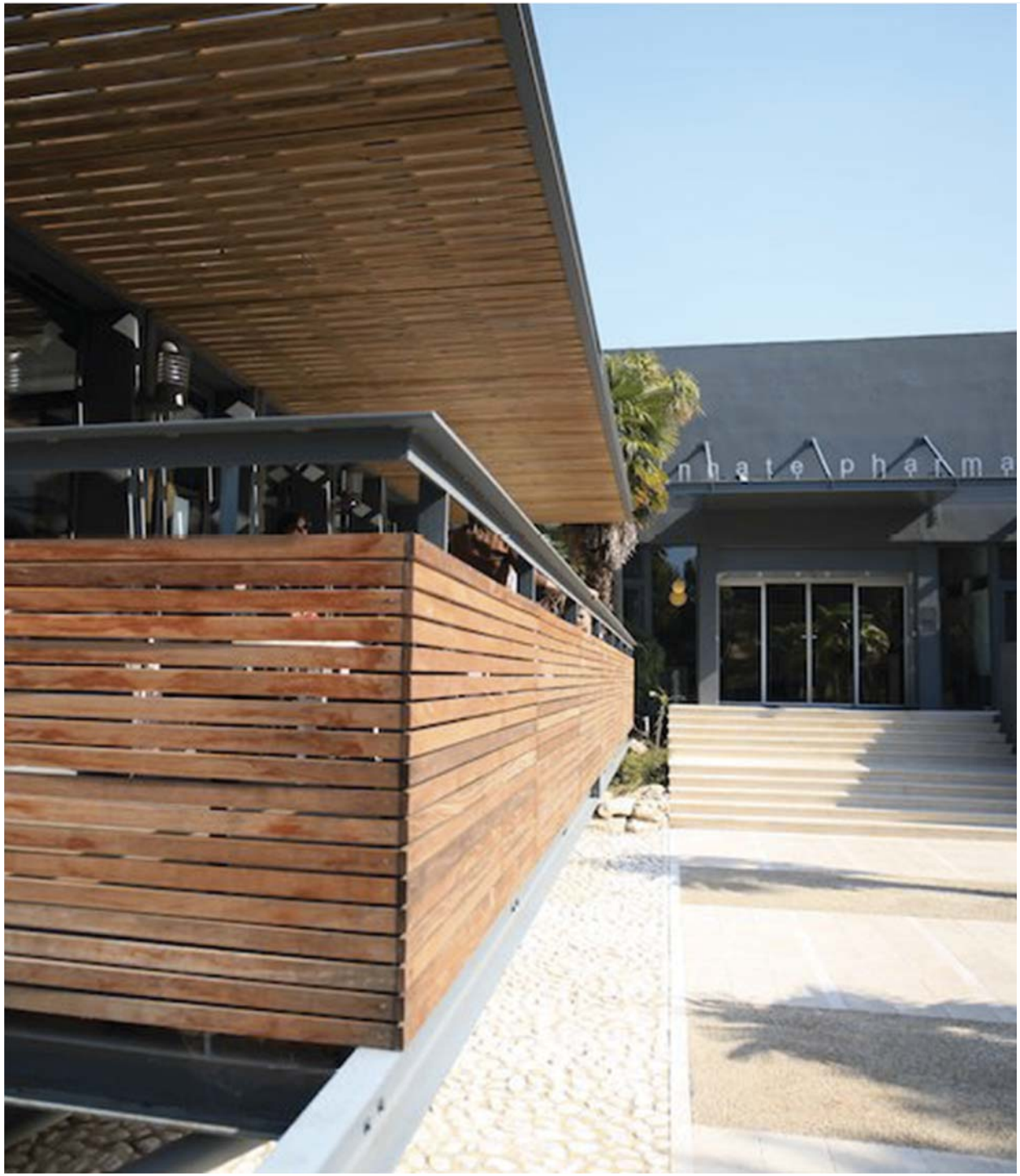
BUILDING A LEADING ONCOLOGY COMPANY FOCUSED ON INNATE IMMUNITY

Investment Summary

- Differentiated and novel science in immuno-oncology
- Portfolio of first-in-class antibodies
- Partnerships with leading immuno-oncology companies
- Strategy to become a fully-integrated biopharma company
- Strong financial position and management team to execute on the business plan
- Key news flow catalysts on horizon

Key Catalysts

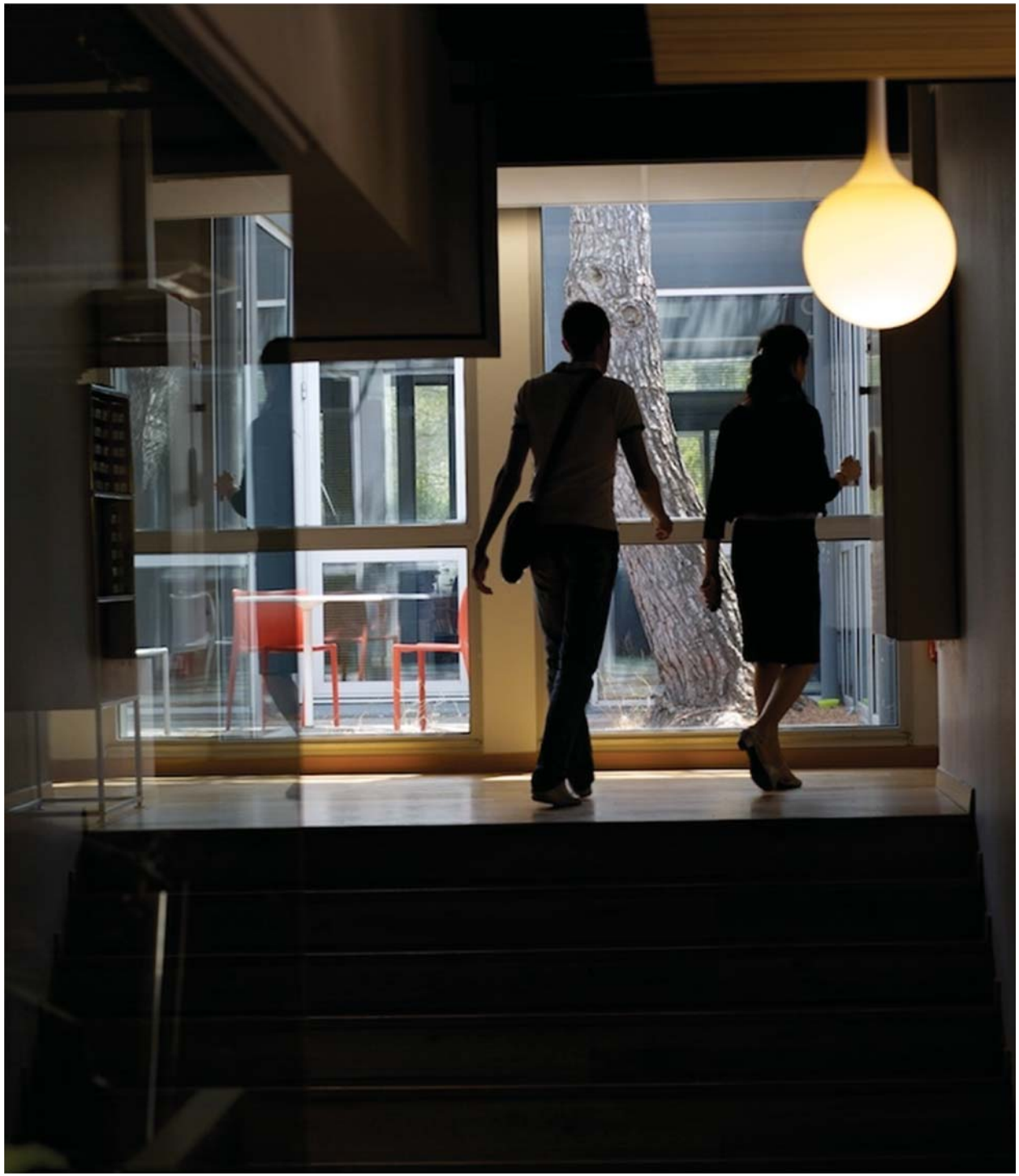
- 2016: Start of lirilumab clinical data read-out. EffiKIR Ph II data expected 2H16
- 2017: Start of monalizumab clinical data read-out; broadening of clinical program
- IPH4102 clinical data expected late 2017 / 2018
- Progress and expansion of early proprietary pipeline
  - > IPH4301 in preclinical development
  - > Two candidates targeting adenosine pathway, IPH52 and anti-CD73 in discovery
- Progress update on bispecific NK Cell Engager development



INVESTOR RELATIONS

Laure-Hélène Mercier
Sr Director, Investor relations

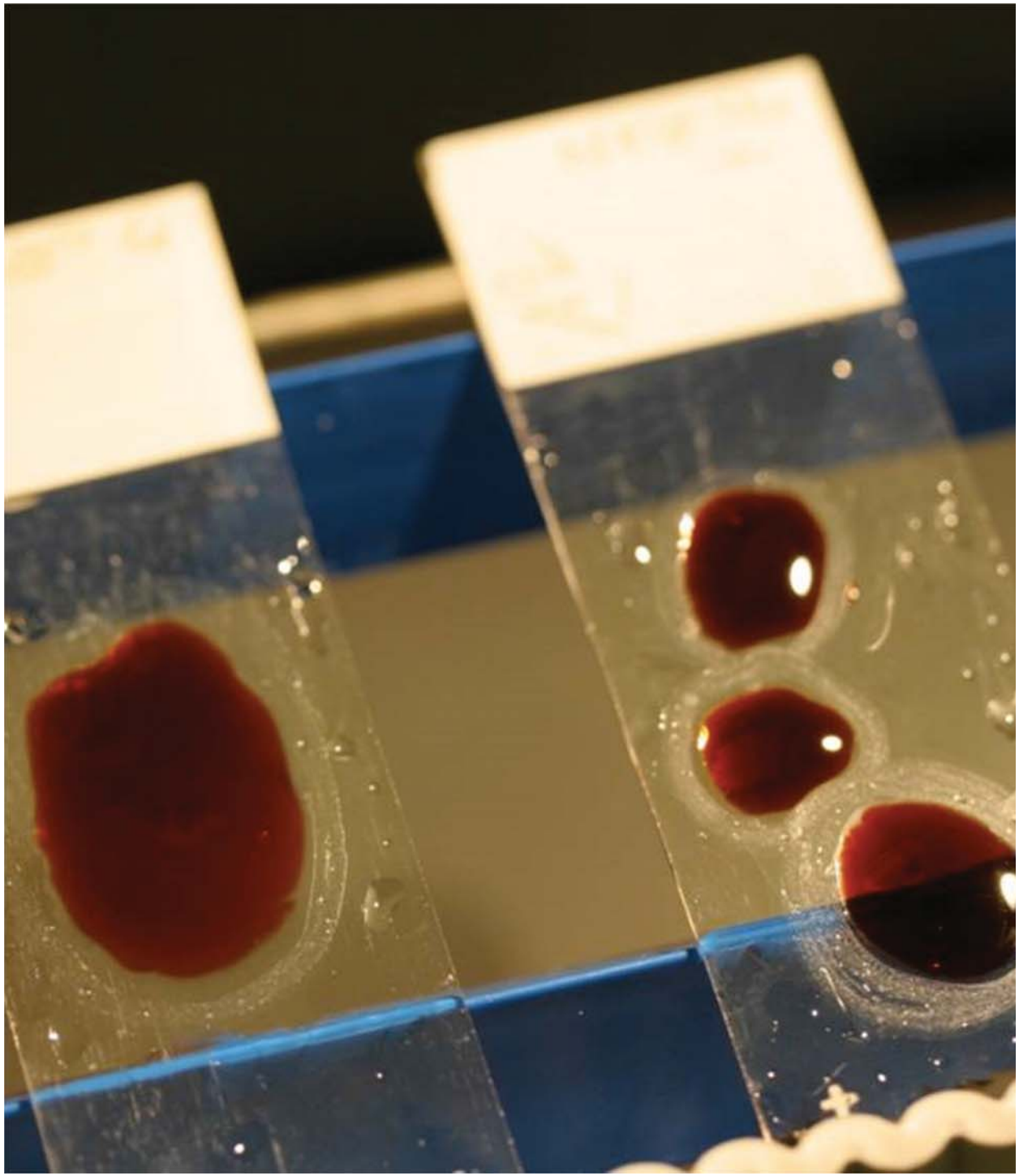
investors@innate-pharma.com
Tel: +33 (0)4 30 30 30 87



APPENDIX

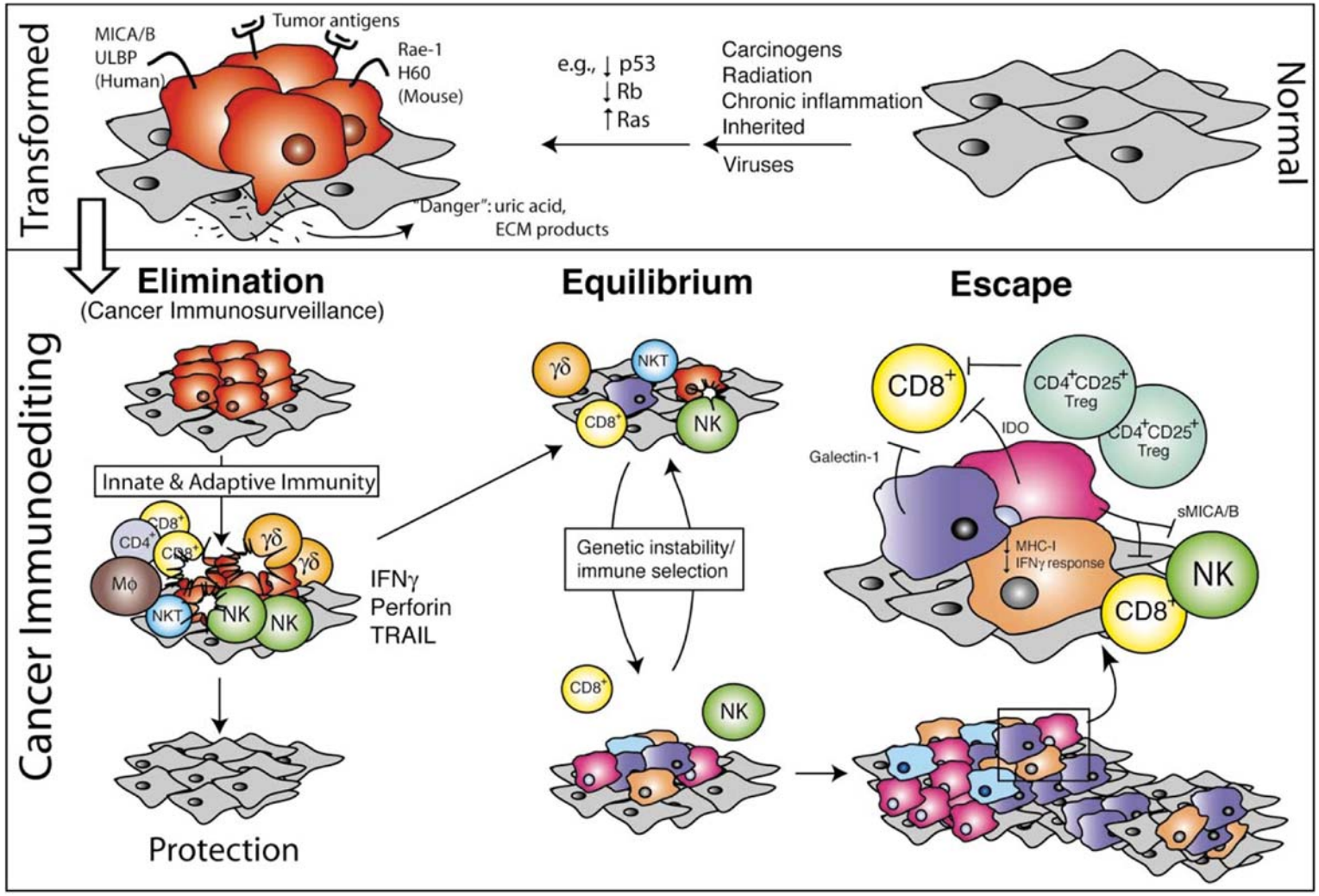
FINANCIAL HIGHLIGHTS
STRONG FINANCIAL POSITION

	Year ended December 31	
In thousand euros (IFRS)	**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)
Cash, cash equivalents and financial instruments	**273,704**	**69,238**
Total financial liabilities	3,754	4,206



NK CELLS
APPENDIX

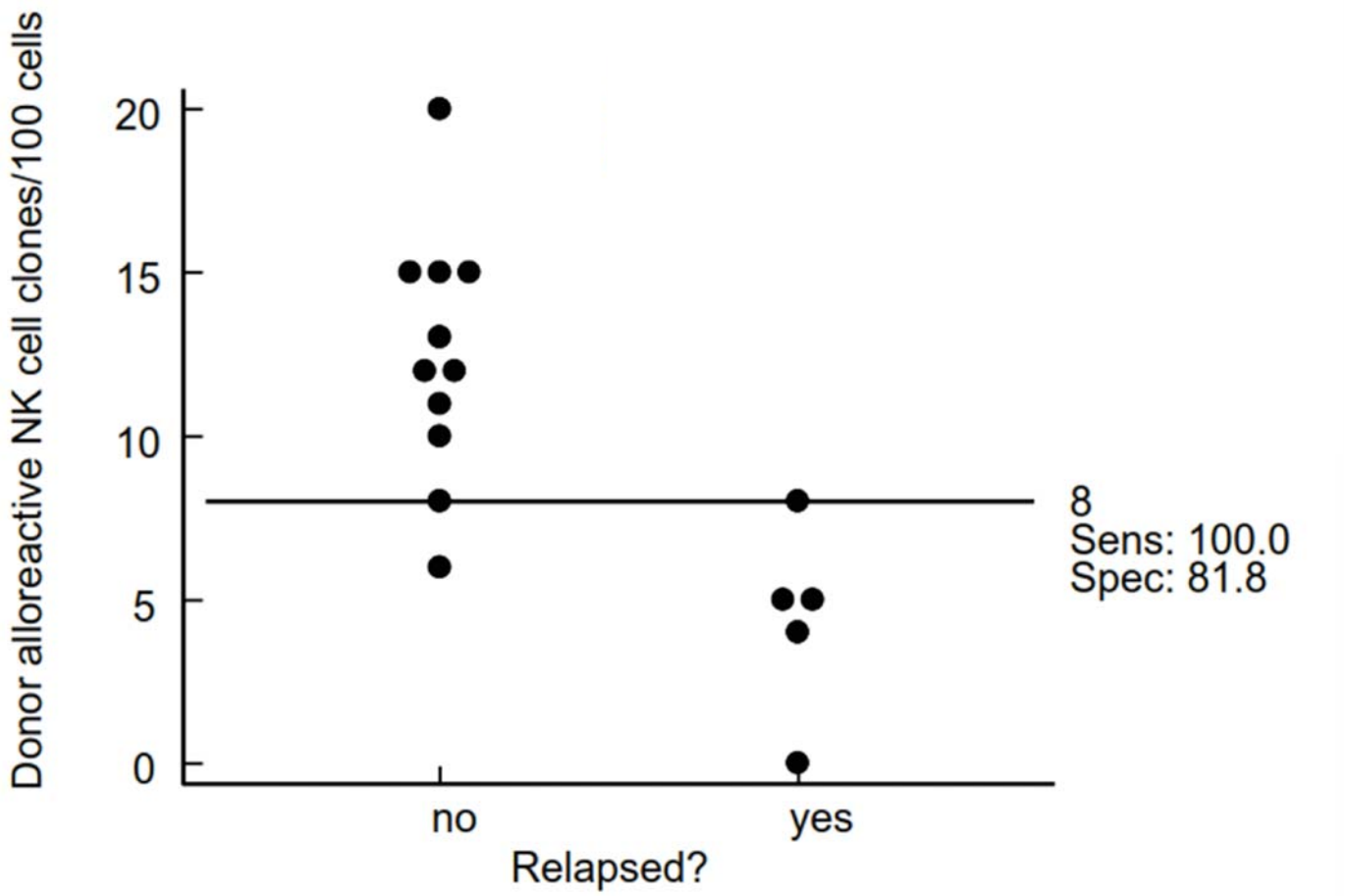
TUMOR IMMUNO-SURVEILLANCE INVOLVES COOPERATION BETWEEN INNATE AND ADAPTIVE IMMUNE CELLS



Dunn, Old and Schreiber. Immunity 2004

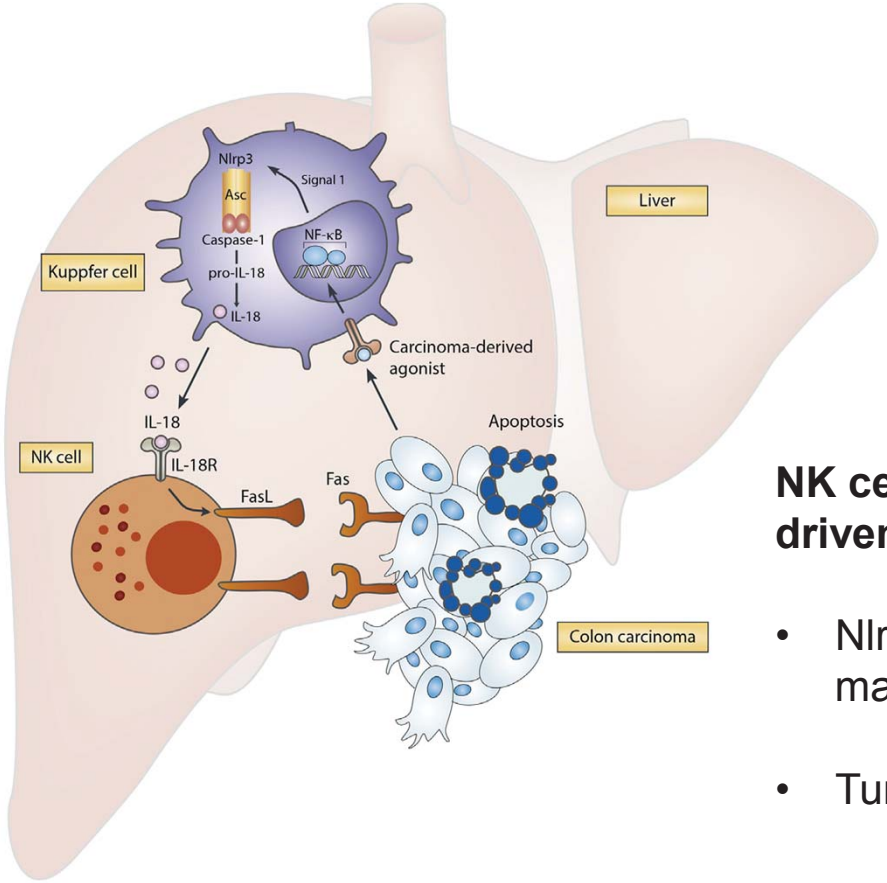
INFUSION OF NK CELLS CAN PREVENT RELAPSE IN ELDERLY AML PATIENTS IN COMPLETE REMISSION

DEPENDS ON SUFFICIENT NUMBERS OF KIR-MISMATCHED NK CELLS



Curti et al. 2016. Clin Cancer Res

IN SOME MODELS, NK CELLS CONTROL TUMOR GROWTH WITHOUT A NEED FOR T CELLS



NK cell control of colon cancer liver metastasis driven by an innate immune circuit in mice:

- Nlrp3 inflammasome-induced IL-18 promote maturation and tumor killing by NK cells
- Tumor control depends on NK, but not T or B cells

Dupaul-Chicoine et al. Immunity 2015

CANCER IMMUNOTHERAPY: APPROACHES BOOSTING NK CELLS

TARGETED RECEPTORS ON NK CELLS

REVIEWS

NK cells and cancer: you can teach innate cells new tricks

Maelig G. Morvan and Lewis L. Lanier

Abstract | Natural killer (NK) cells are the prototype innate lymphoid cells endowed with potent cytolytic function that provide host defence against microbial infection and tumours. Here, we review evidence for the role of NK cells in immune surveillance against cancer and highlight new therapeutic approaches for targeting NK cells in the treatment of cancer.

NATURE REVIEWS | CANCER VOLUME 16 | JANUARY 2016 | 7

Innate Pharma

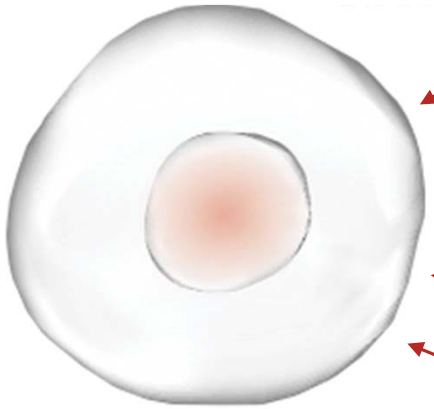
Checkpoint inhibitors:

Lirilumab | IPH/BMS

Monalizumab | IPH/AZN

Bispecifics

NKp46-targeting bispecifics



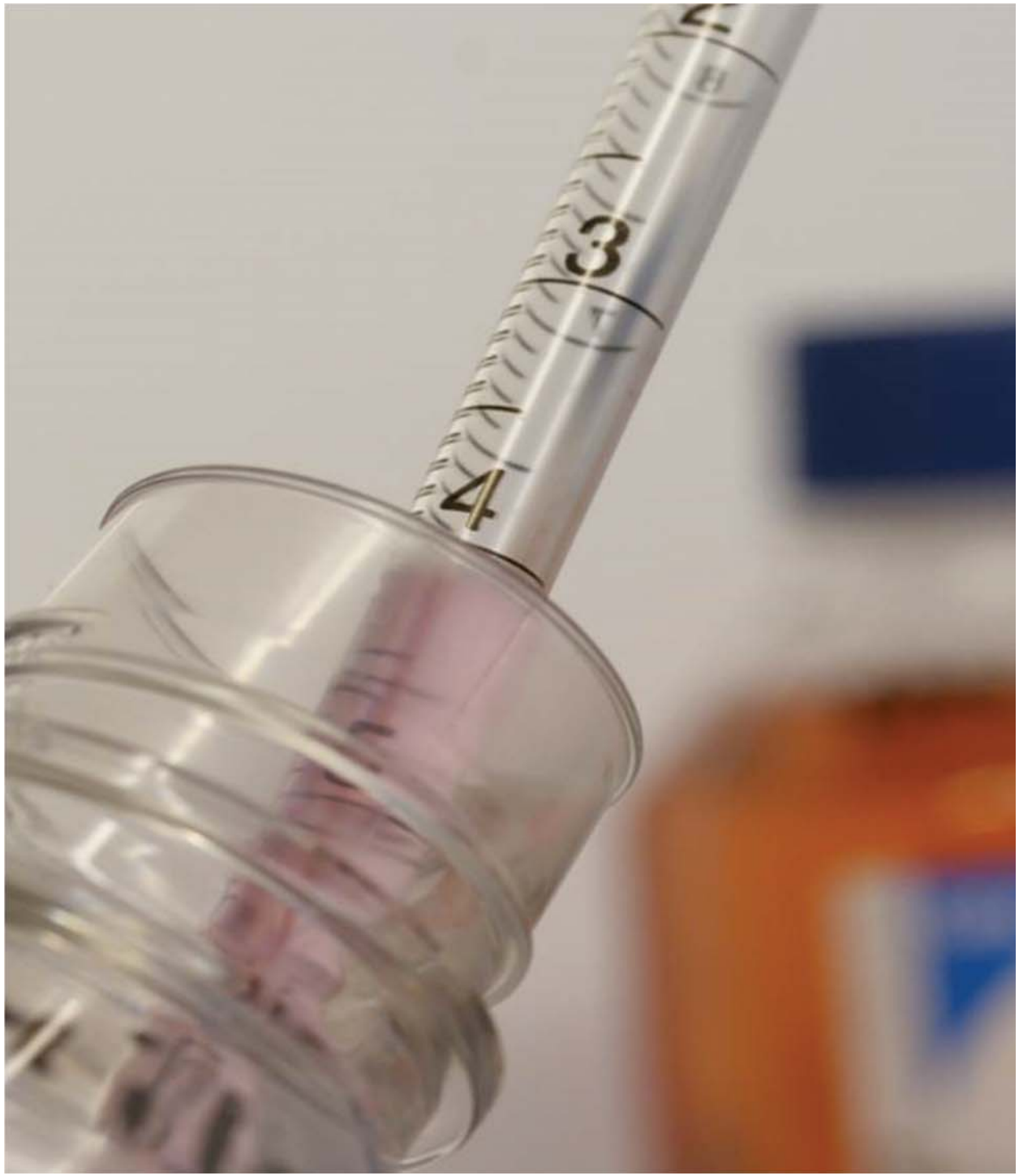
Anti-CD137 | BMS, **Agonist mAB**

CD16-targeting bispecifics | Affimed **Bispecifics**

IL-12 | Celsion, **Cytokine**

CEA-IL-2 | Roche, **Antibody-IL2 fusion proteins**

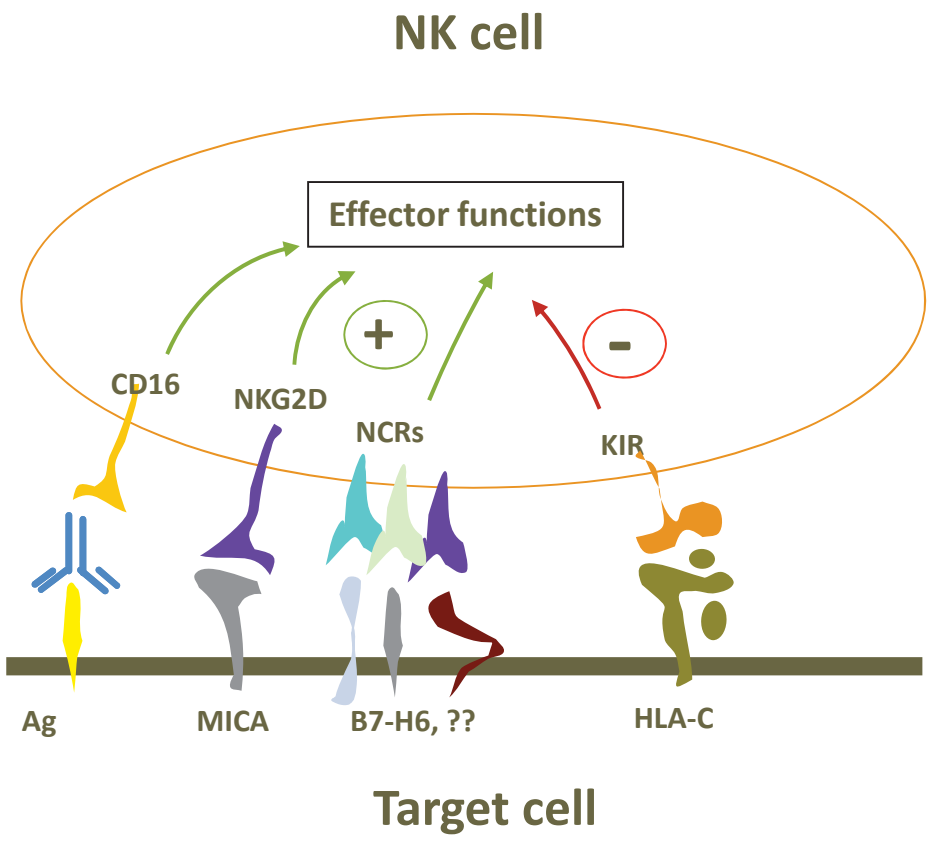
CARNK cells | NaNKwest, Celyad, Cytomx, **Cell therapy**

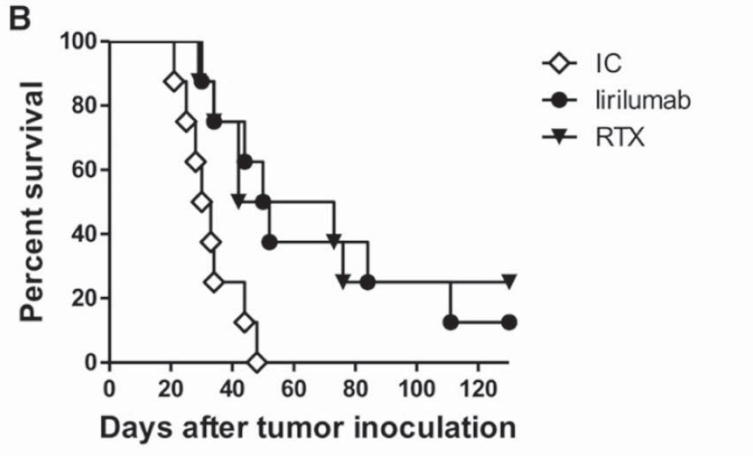


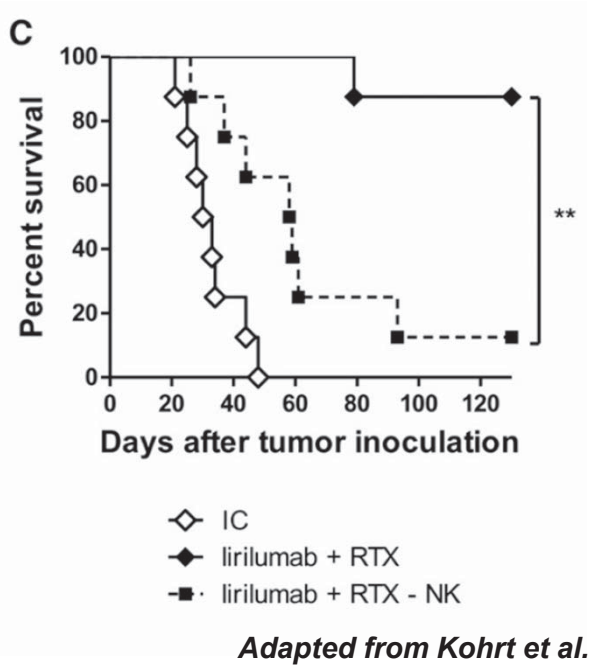
LIRILUMAB
APPENDIX

NK CHECKPOINT RECEPTORS INHIBIT ADCC

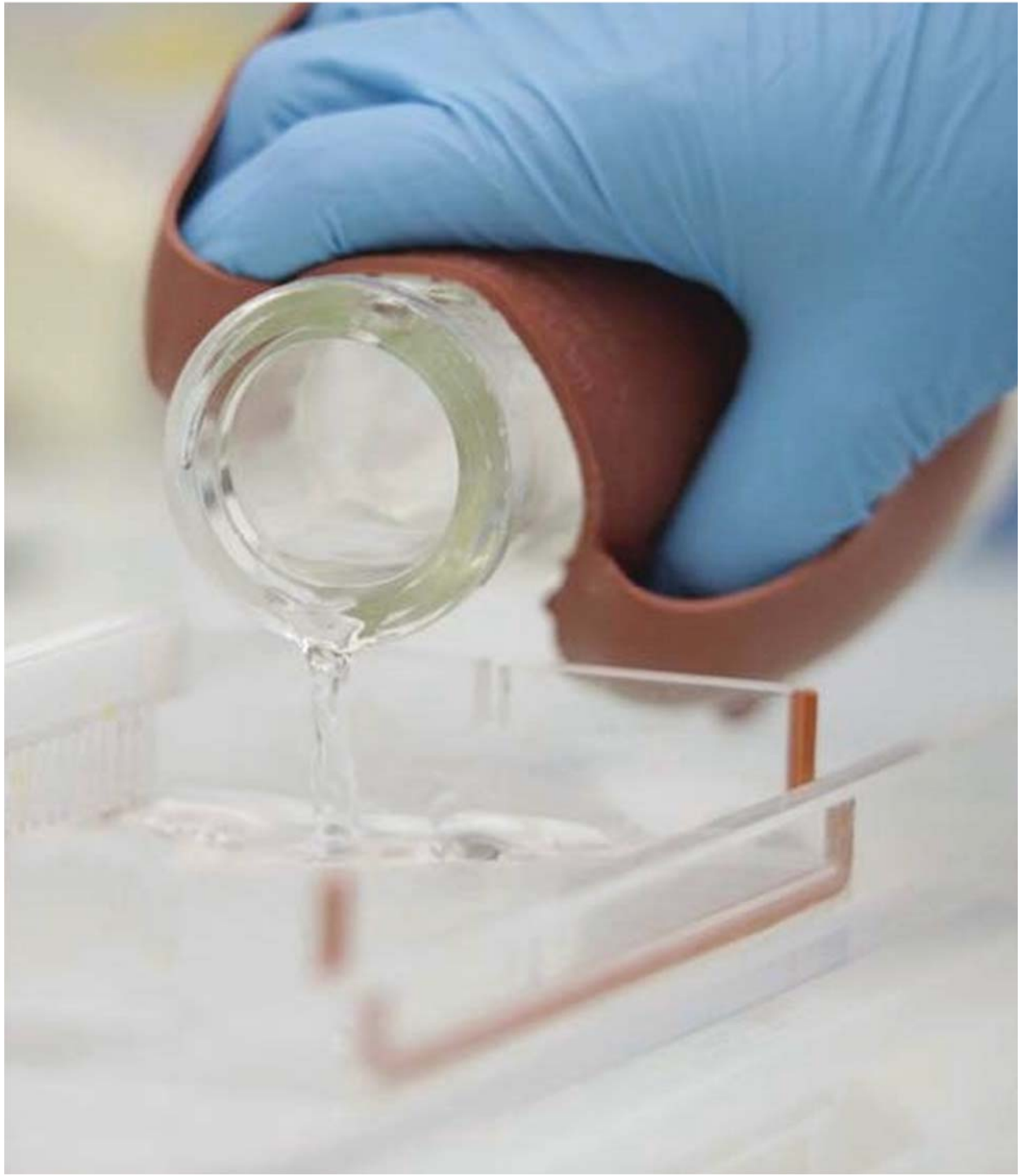
RITUXIMAB EFFICACY CAN BE ENHANCED BY LIRILUMAB







Adapted from Kohrt et al. Blood 2014

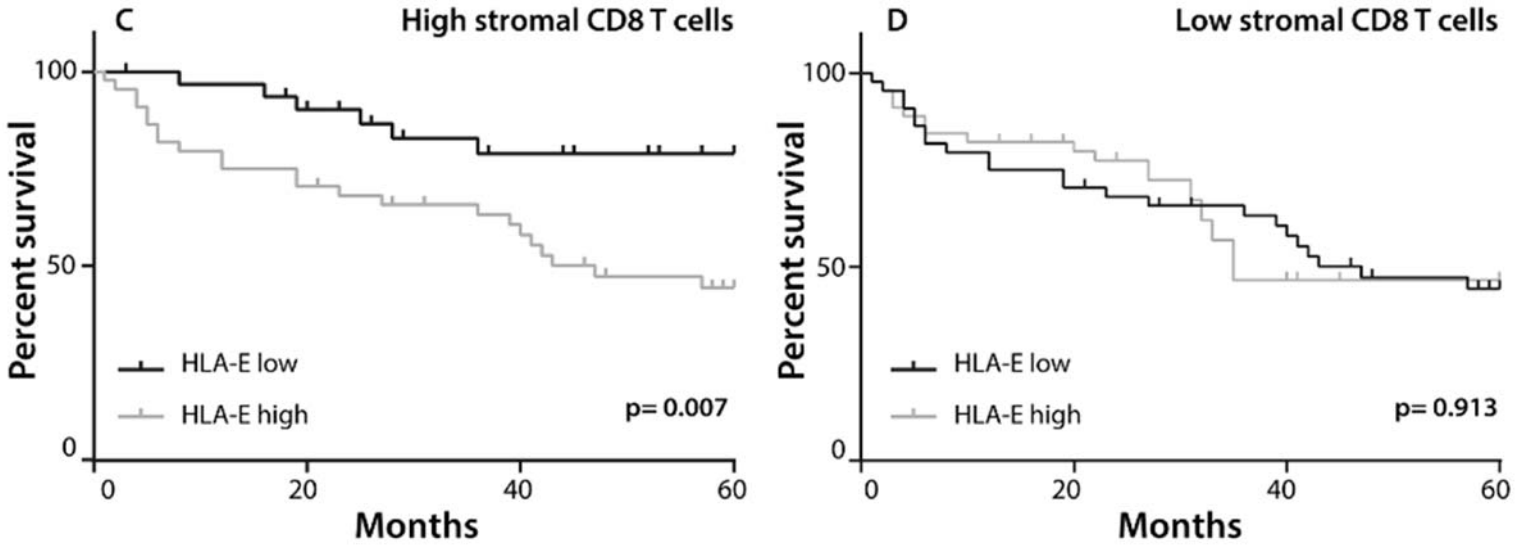


MONALIZUMAB
APPENDIX

HLA-E EXPRESSION CONFERS POOR PROGNOSIS IN SOME CANCERS

The example of lung adenocarcinoma:

HLA-E (number, %)		
Low	55	(28%)
High	142	(72%)



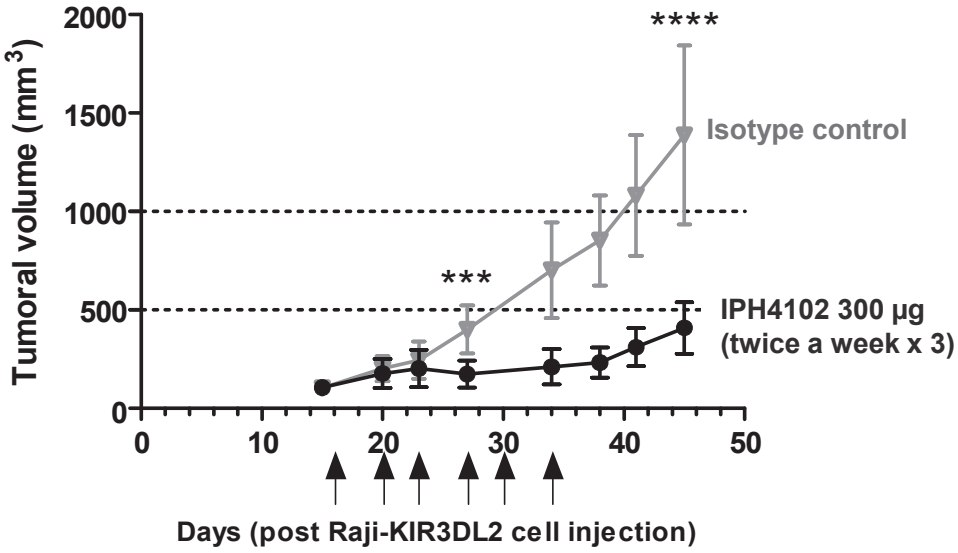
Van der Burg et al Oncotarget 2015

IPH4102
IPH4301
IPH52
APPENDIX

IPH4102 IS A FIRST-IN-CLASS CYTOTOXICITY-INDUCING ANTIBODY
POTENT ANTITUMOR ACTIVITY IN MODELS OF ADVANCED CTCL

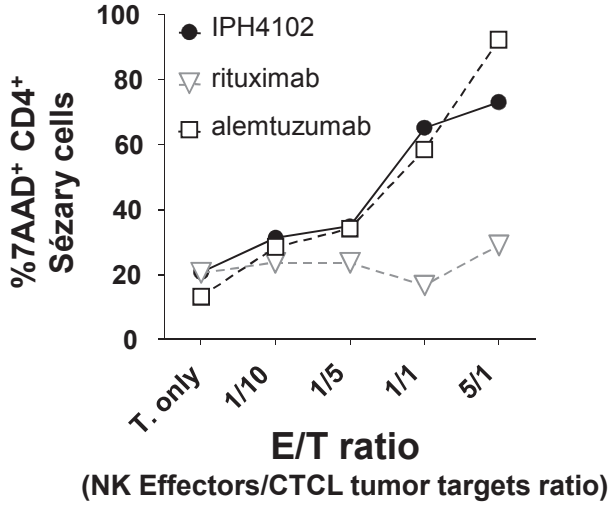
- Humanized cytotoxic IgG1

RAJI-KIR3DL2 SC xenograft model



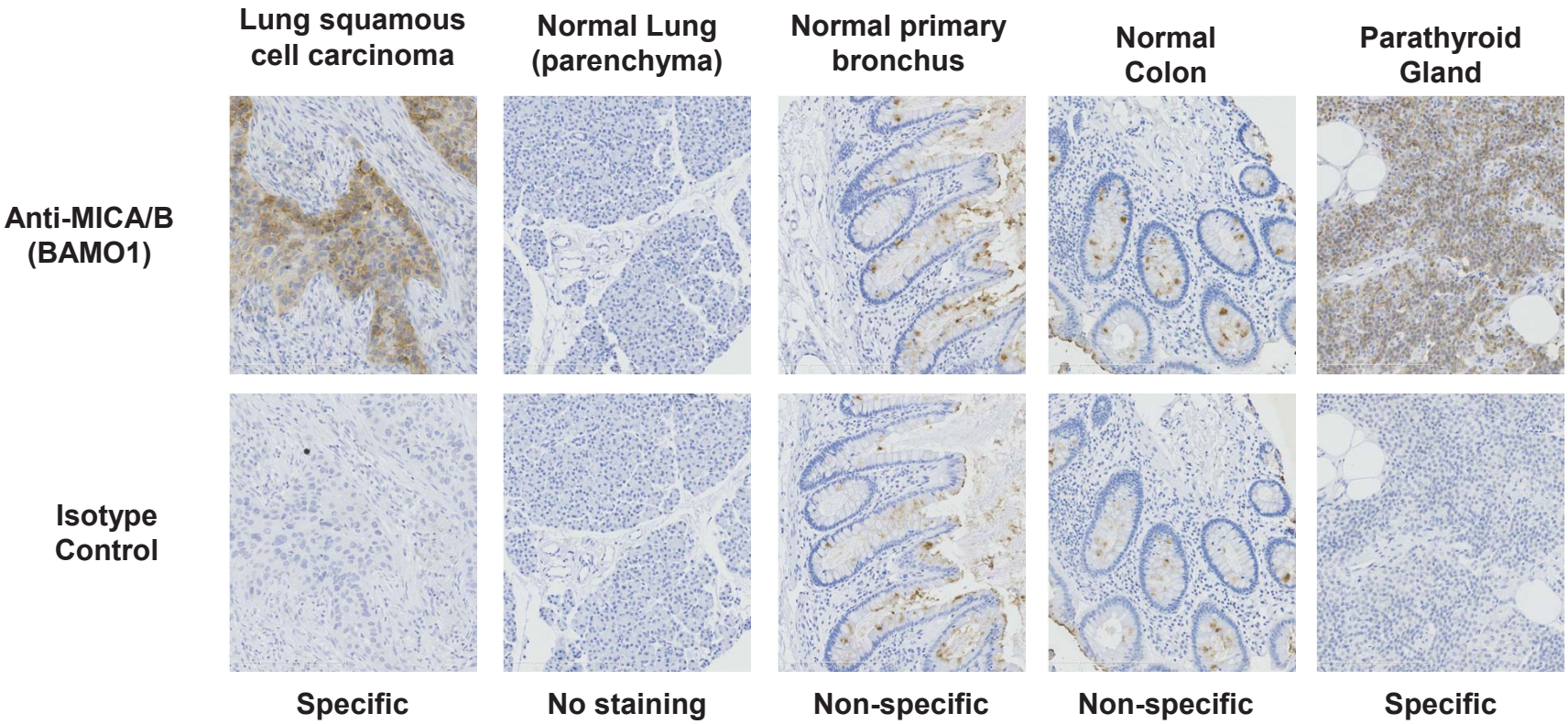
Autologous ADCC with CTCL patient cells

Patient #10 (representative of n = 15)



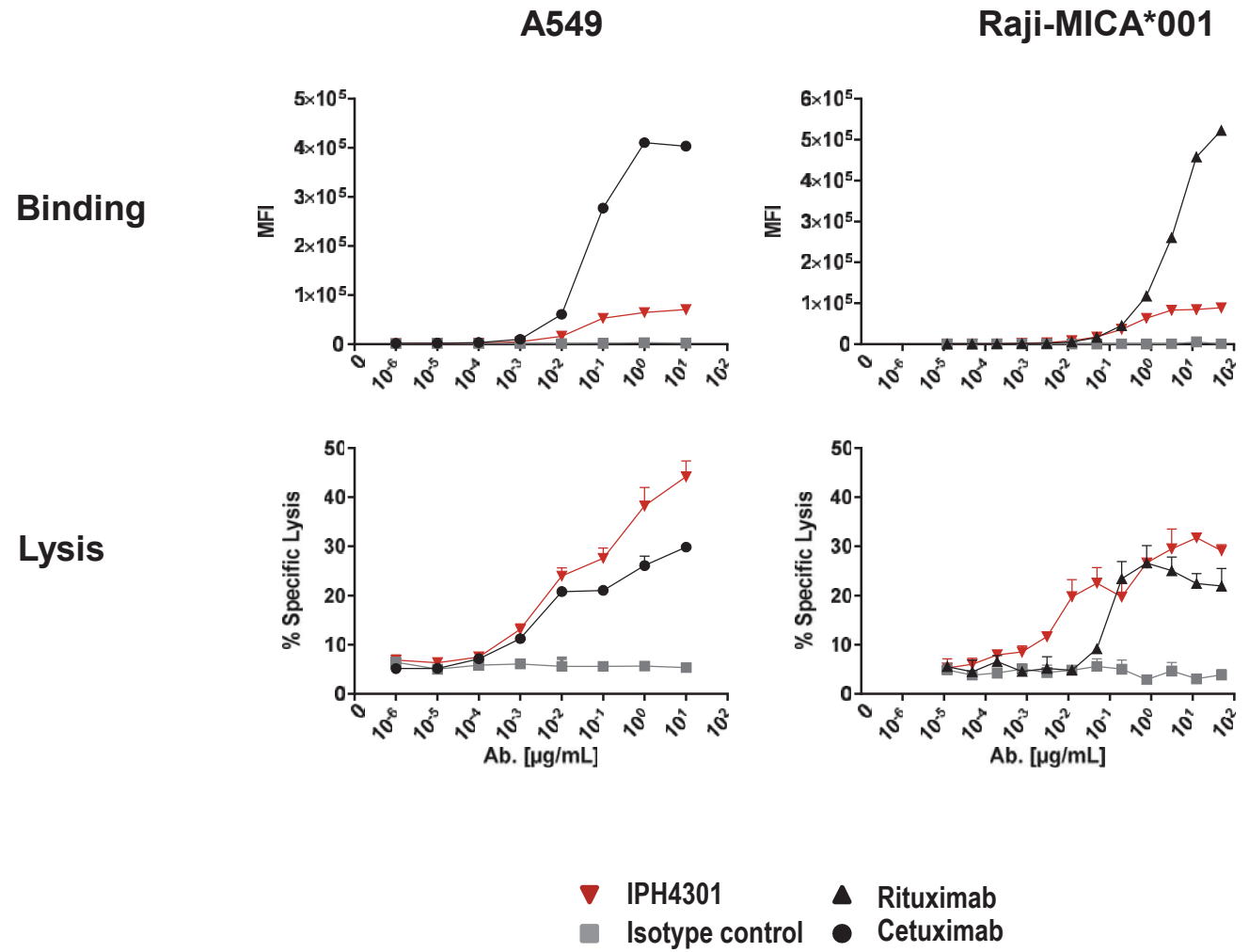
http://innate-pharma.com/sites/default/files/150926_eortc_bagot_neil_smith_2.pdf
http://innate-pharma.com/sites/default/files/20151002_iph4102-101_study.pdf
Collaboration with St Louis Hospital, Paris

PARATHYROID GLAND IS THE ONLY NORMAL TISSUE WITH SPECIFIC, CONSISTENT MICA/B STAINING



IHC analysis of FDA-approved 72-tissue panel (3 donors pr tissue)
FFPE samples were stained with Bam01 mAb using an optimized and validated protocol
Results analyzed by external pathologist

IPH4301: POTENT ADCC BY RESTING PRIMARY HUMAN NK CELLS

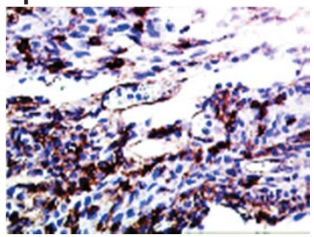


PBMC from healthy donors – E/T = 200/1

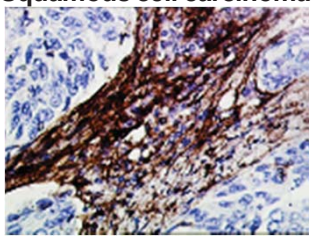
IPH52
NOVEL, POTENT ANTI-CD39 ANTIBODY

- CD39 is expressed in several human cancers, including head & neck, lung, cervical, esophageal, sarcoma, liver, kidney, pancreatic, thyroid, endometrial tumors, as well as in lymphoma and melanoma

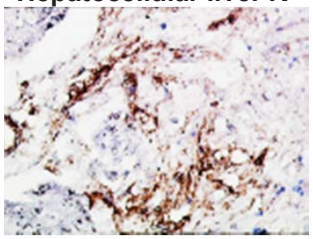
Head & neck
Squamous Cell Carcinoma



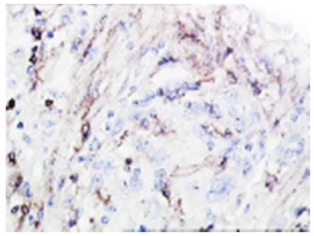
Cervix
Squamous cell carcinoma



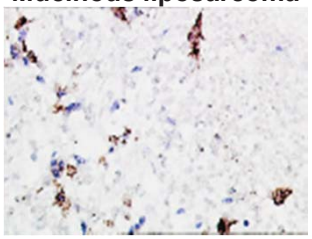
Liver
Hepatocellular liver K



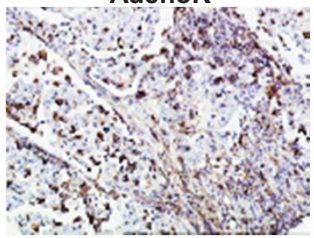
Pancreas
Adenocarcinoma



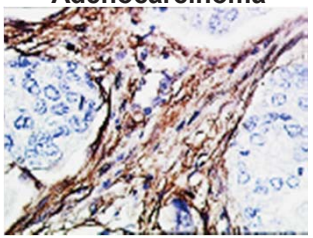
Soft tissue
Mucinous liposarcoma



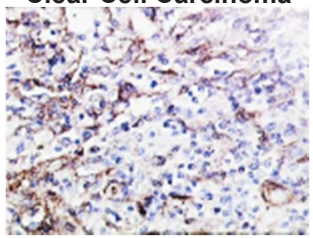
Lung
AdenoK



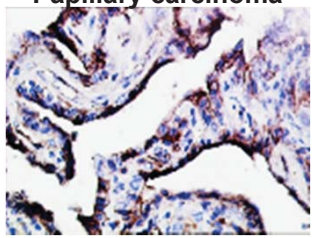
Esophagus
Adenocarcinoma



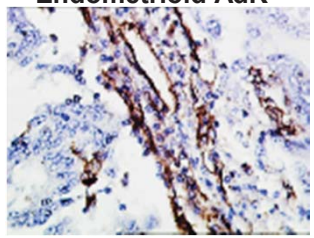
Kidney
Clear Cell Carcinoma



Thyroid
Papillary carcinoma

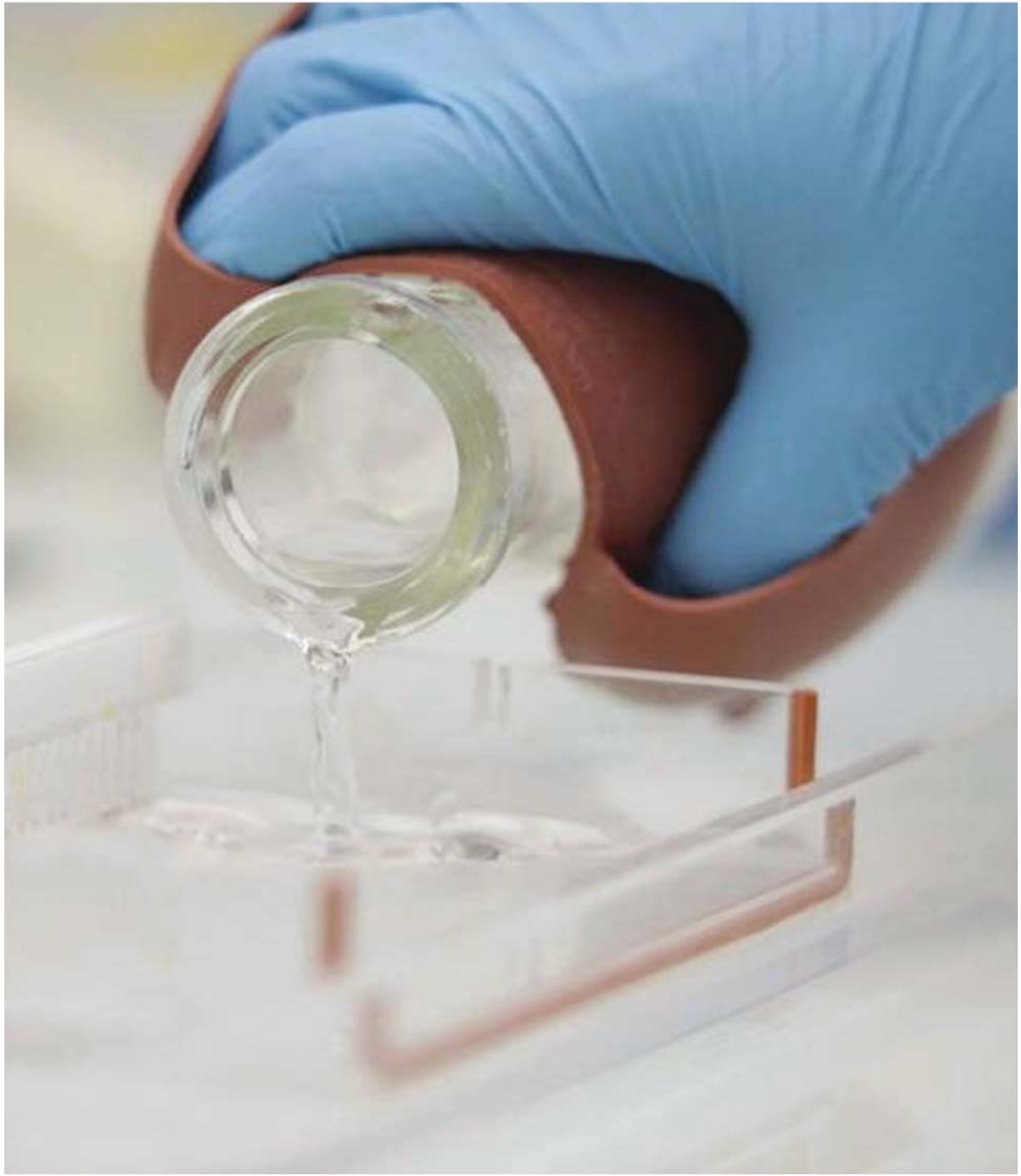


Uterus
Endometrioid AdK



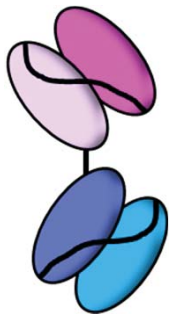
- IPH52 is a humanized anti-CD39 mAb
  - > Aims at preventing production of immunosuppressive Ado and promoting the accumulation of ATP in the tumor microenvironment
  - > May stimulate anti-tumor immunity across a wide range of tumors

Internal data



TECHNOLOGIES
APPENDIX

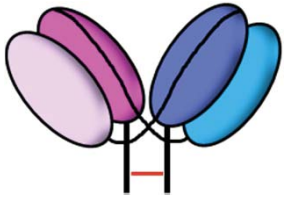
BISPECIFIC ANTIBODIES:
A BOOMING FIELD, VALIDATED BY APPROVAL OF BLINCYTO



BITE
Amgen

ScFV-tandem
Monovalent

CD19/CD3
Approved in ALL

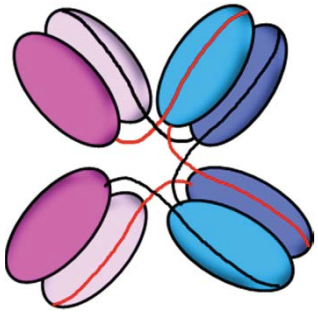


DART
Macrogenics

ScFV-hybrid
Monovalent

CD123/CD3
Phase I AML

Gp33/CD3
Phase I solid tumors

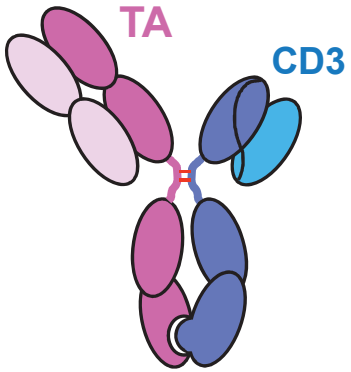


TandAb
Affimed

ScFV-hybrid
Bivalent

CD19-CD3
Phase 1 NHL-ALL

CD30-CD16 NK engager
Phase II HL



Xencor

ScFV-Fc Knobs-in-Holes
Monovalent

CD3 T cell engager

BLINATUMOMAB: CD3-CD19 BISPECIFIC T CELL ENGAGER

VALIDATION OF BISPECIFIC CONCEPT - BUT WITH SOME TOXICITY ISSUES

WARNING: CYTOKINE RELEASE SYNDROME and NEUROLOGICAL TOXICITIES

See full prescribing information for complete boxed warning.

- **Cytokine Release Syndrome (CRS), which may be life-threatening or fatal, occurred in patients receiving BLINCYTO. Interrupt or discontinue BLINCYTO as recommended. (2.3), (5.1)**
- **Neurological toxicities, which may be severe, life-threatening, or fatal, occurred in patients receiving BLINCYTO. Interrupt or discontinue BLINCYTO as recommended. (2.3), (5.2)**

Table 2 Main toxicities observed in clinical trials in R/R acute lymphoblastic leukemia

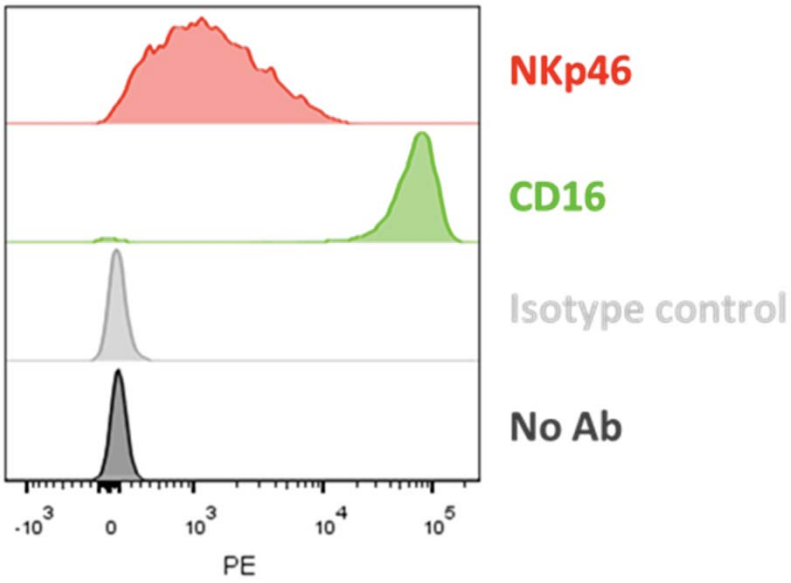
Trial (reference)	Blinatumomab schedule	Most common adverse events	Most common grade 3–4 adverse events	Fatal adverse events
R/R Phase II GMALL trial (n=36)[22]	Varied by cohort 5 µg/m²/day in week 1 and 15 µg/m²/day thereafter in the extension phase	Pyrexia, fatigue, headache, tremor, leukopenia	Transient leukopenia and thrombocytopenia	6
R/R Phase II international confirmatory trial (n=189)[25]	First cycle: 9 µg/m²/day in week 1 and 28 µg/m²/day thereafter Subsequent cycles: 28 µg/m²/day ×4 weeks	Pyrexia, headache, febrile neutropenia	Febrile neutropenia, neutropenia, anemia	28 → 15%
R/R pediatric Phase II trial (n=39)[27]	First cycle: 5 µg/m²/day for 7 days, then 15 µg/m²/day Subsequent cycles: 15 µg/m²/day	Pyrexia, anemia, nausea, headache Increased AST and ALT	Anemia, pyrexia, increased AST and ALT, febrile neutropenia	0

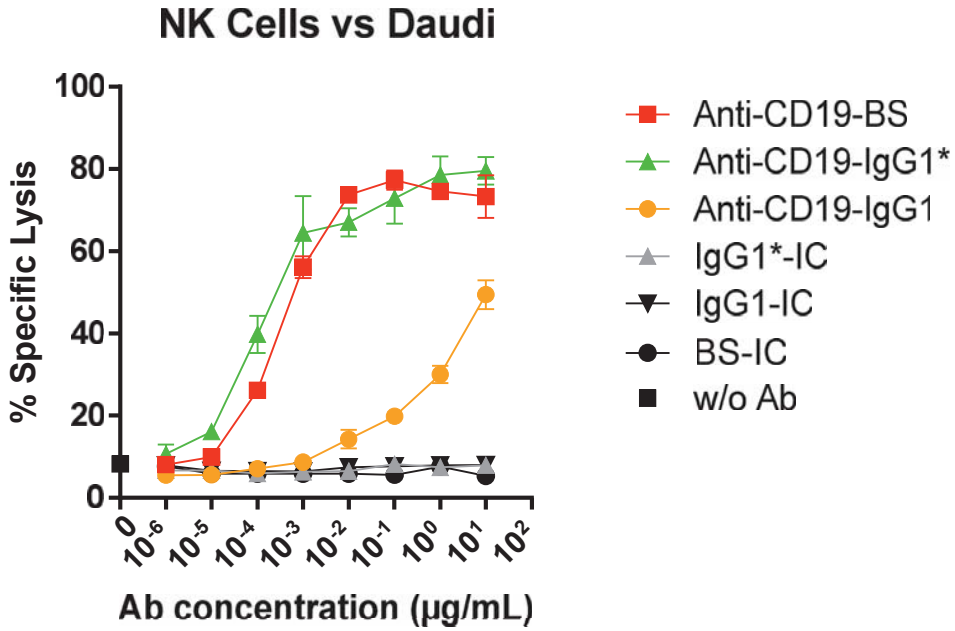
Abbreviations: R/R, relapsed/refractory; GMALL, German Multicenter Adult Acute Lymphoblastic Leukemia Group; AST, aspartate aminotransferase; ALT, alanine aminotransferase.

J-M Ribera et al, OncoTargets and Therapy, 2015

NKp46 BISPECIFICS

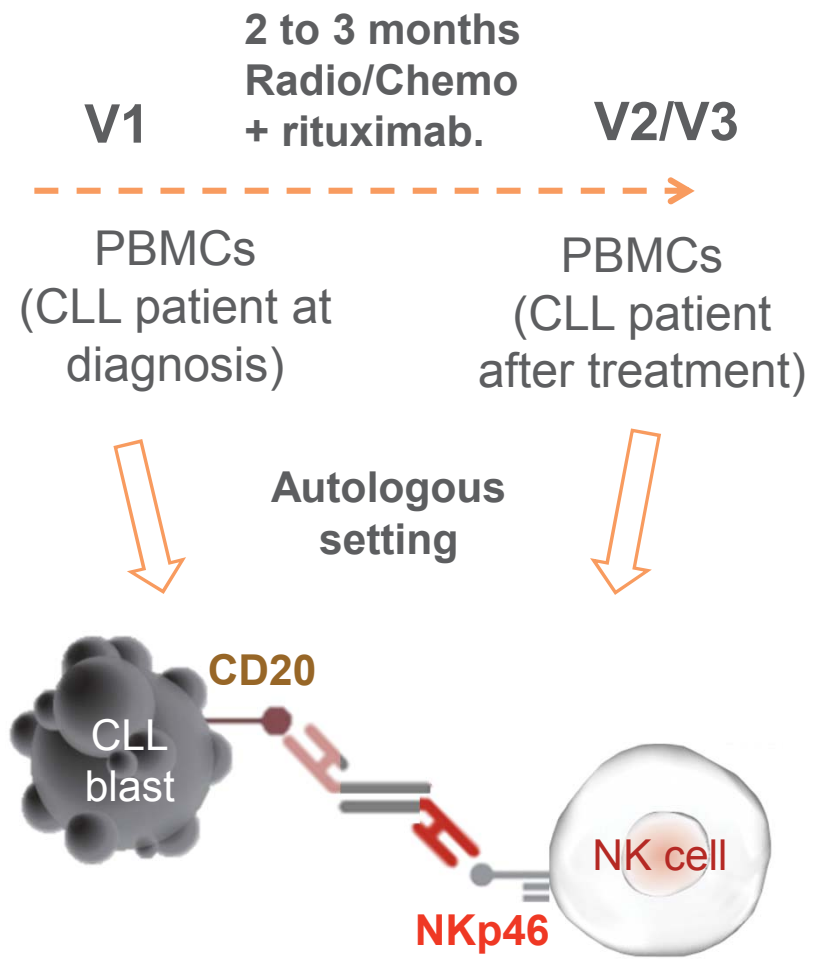
POTENT KILLING BY PRIMARY BLOOD NK CELLS OF HEALTHY DONORS, DESPITE MUCH GREATER CD16 EXPRESSION



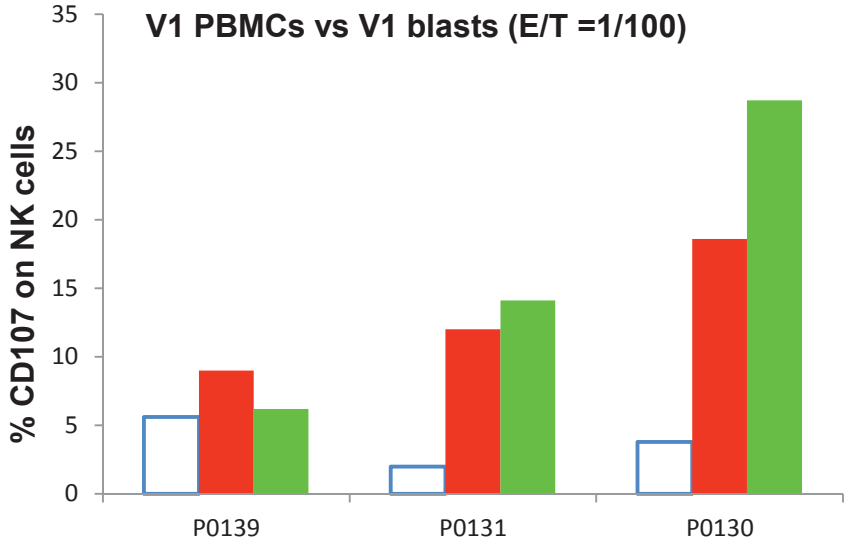


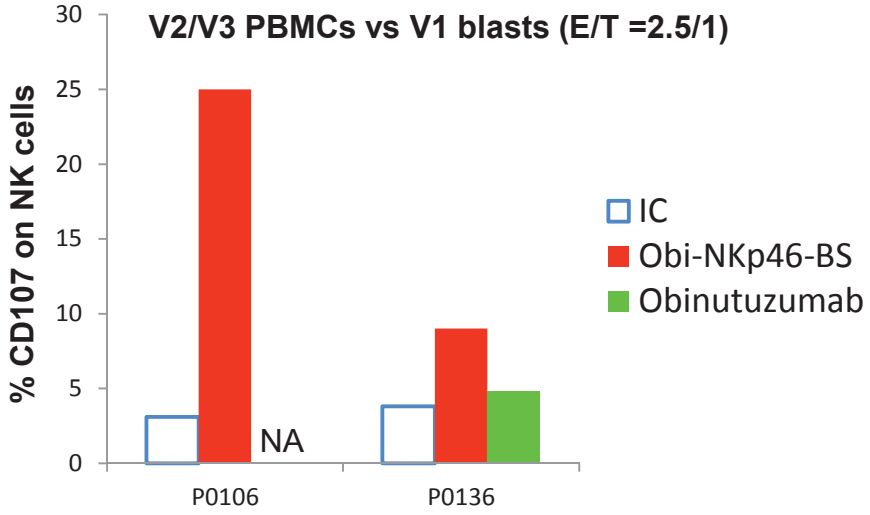
Anti-CD19 binding domain was derived from blinatumomab (BITE)

NKP46 BISPECIFICS INDUCE KILLING OF CLL BLASTS BY AUTOLOGOUS PATIENT NK CELLS

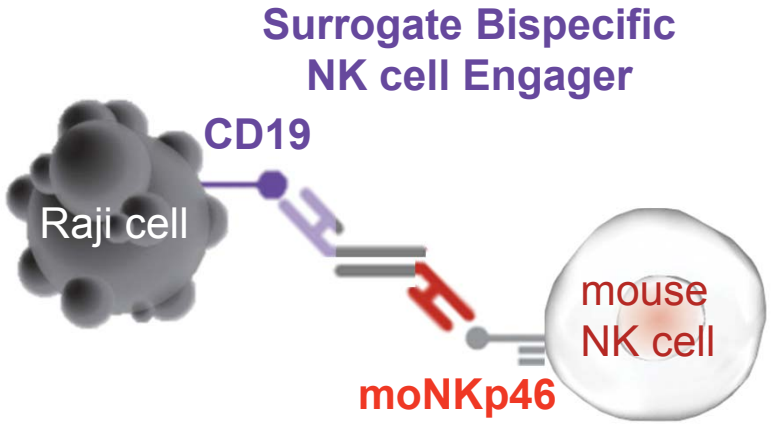


Bispecific NK cell Engager

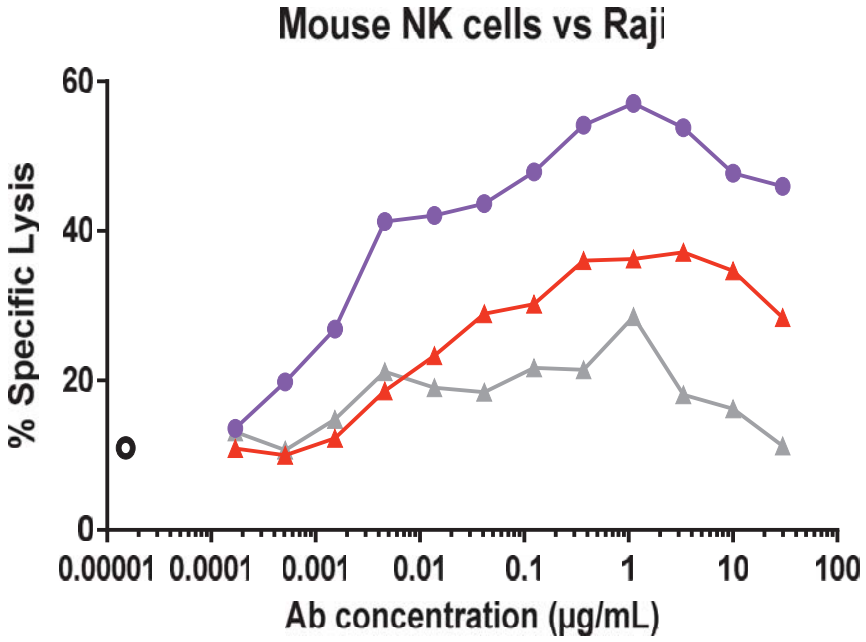




SURROGATE BISPECIFIC
ACTIVATION OF MOUSE NK CELLS *EX VIVO*



Anti-moNKp46 antibody:
Mousified version of a rat Anti-mouse NKp46 antibody



Effectors:
Mouse NK cells purified from pIC treated mice
Targets:
Raji labelled with ^{51}Cr
E/T = 3/1