innate pharma

R&D DAY 2018

LONDON, MARCH 8

IPH LISTED EURONEXT

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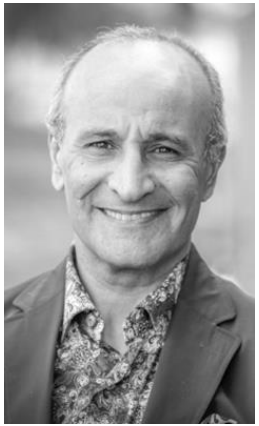
TODAY'S SPEAKERS



Mondher MAHJOUBI, MD,

Chief Executive Officer
Innate Pharma

Eric VIVIER, DVM, PhD

Chief Scientific Officer
Innate Pharma

Pierre DODION, MD, MBA,

Chief Medical Officer
Innate Pharma

Julia SCARISBRICK, MD,

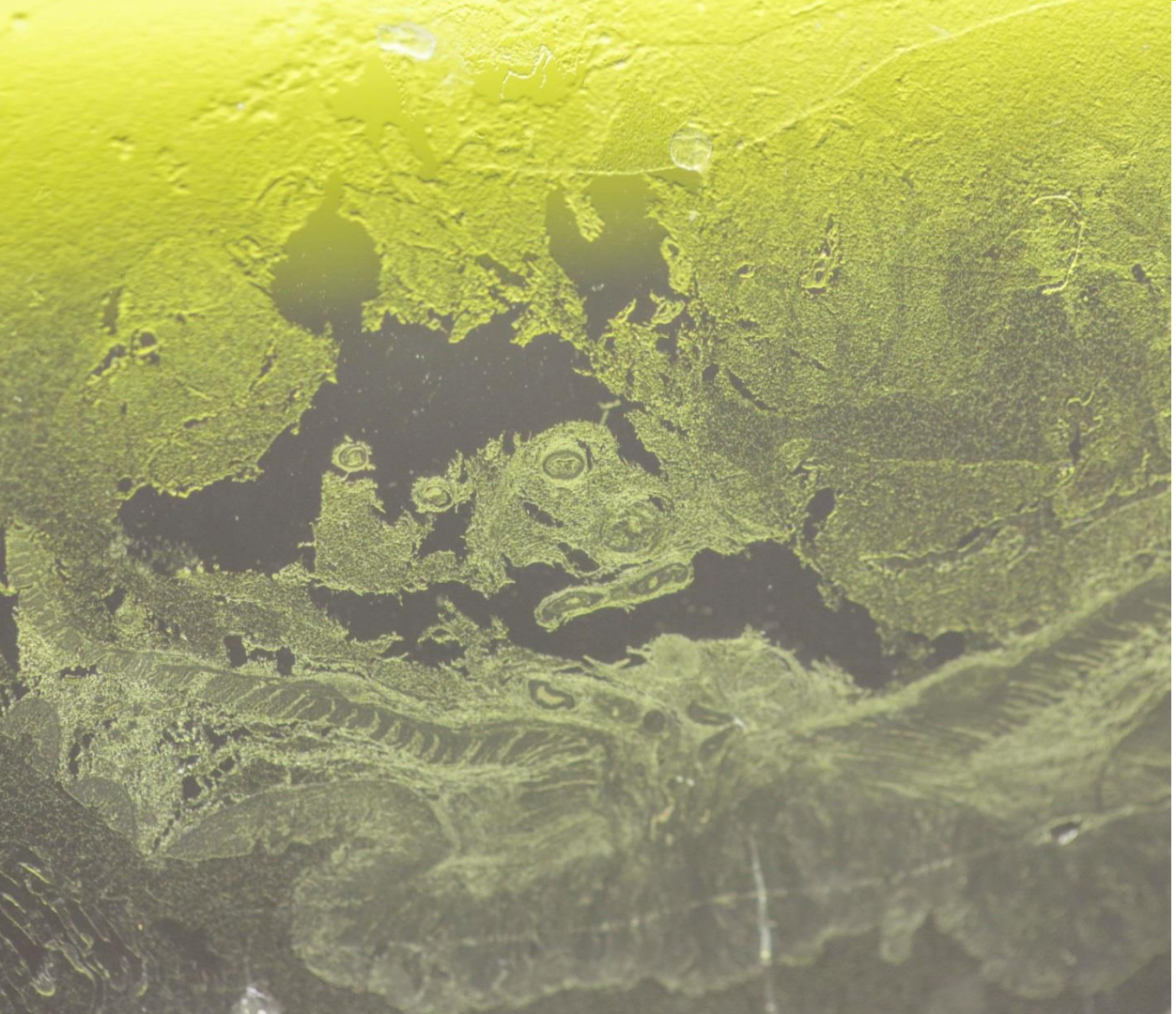
Dermatologist & Lead, Cutaneous Lymphoma University Hospitals Birmingham NHS Foundation Trust

Mohammed DAR, MD,

VP Clinical Development Oncology, AstraZeneca/MedImmune

AGENDA

1. **STRATEGY INTRODUCTION** – MONDHER MAHJOUBI
2. **BUILDING AN INNOVATIVE AND DIFFERENTIATED PIPELINE** – ERIC VIVIER
3. **PROPRIETARY PIPELINE** – PIERRE DODION
   - > IPH5401 – POTENTIAL TO UNLOCK THE IMMUNE RESPONSE
   - > IPH4102 – NEW THERAPEUTIC OPTION FOR T-CELL LYMPHOMA – JULIA SCARISBRICK
4. **PARTNERED PIPELINE**
   - > MONALIZUMAB – COMBINATION STRATEGY OPPORTUNITY – MOHAMMED DAR
5. **MARKET POTENTIAL AND PIPELINE NEWSFLOW** – MONDHER MAHJOUBI
6. **Q&A**
7. **CLOSING REMARKS**



STRATEGY INTRODUCTION

MONDHER MAHJOUBI

CHIEF EXECUTIVE OFFICER

KEY MESSAGES

- World-class science and technology platform
- Clinical read-outs ahead for monalizumab and IPH4102 programs
- Delivering on IPH5401 with clinical collaborations to accelerate development
- Potential to address large unmet medical needs in cancer
- Financial strength, enabling room for investment

INNATE PHARMA – STRATEGY

SCIENCE DRIVEN ORGANIZATION AND PATIENT CENTRIC COMPANY

Strategic Priorities

- Create **diverse** portfolio of **first** or **best**-in-class IO agents
- **Partner** with leading IO companies to unlock the value of assets with substantial market potential
- Retain more **value** in house and move toward **integrated** biopharma company

INNATE PHARMA – APPROACH

SCIENTIFIC EXCELLENCE AROUND 3 KEY PILLARS

1	2	3
NK cells checkpoints (NKCP)	**Tumor targeting (TAg)**	**Tumor Microenvironment (TME)**

INNATE PHARMA – PIPELINE

FIRST-IN-CLASS IMMUNO-ONCOLOGY (IO) ASSETS

Target Discovery	Drug Discovery	Preclinical	Dose finding	Signal detection	Pivotal
~20 targets or concepts under exploration	Anti-Siglec-9	**IPH52** Anti-CD39	**IPH5401** Anti-C5aR	**Monalizumab** Anti-NKG2A	
	SAN-NKCE-2	**IPH53** Anti-CD73		**Lirilumab** Anti-KIR2DL1,2,3	
	Other undisclosed targets	**IPH4301** Anti-MICA/B		**IPH4102** Anti-KIR3DL2	
		IPH61 SAN-NKCE-1			

INNATE PHARMA – PRIORITIES AND KEY CATALYSTS

Key Value Creation Steps 2018

- **Read-out of current clinical programs**
  - > Monalizumab w/ cetuximab in advanced SCCHN @AACR
  - > Monalizumab w/ durvalumab in solid tumors
  - > Cohort expansion data for IPH4102
- **Preparing next stages of clinical studies**
  - > IPH4102: lifting the full potential in T-Cell lymphomas beyond CTCL
  - > IPH5401 to enter the clinic in oncology in H2; clinical collaborations to secure full development opportunities potential in prioritized indications
  - > Finalize preclinical package for IPH52/53
- **Grow development portfolio, create next generation of product candidates**

FY2017 RESULTS

FINANCIAL STRENGTH, ENABLING INVESTMENTS IN FUTURE GROWTH

Revenue*:	**€44m**
Op. expenses:	**€84m**
Cash position:	**€177m**

- Mainly from industrial partnerships
- Increase in R&D expenses support clinical development of IPH4102 and monalizumab
- 2017 cash burn €54m**
- Strong cash position to invest in development pipeline

*revenue and other income
** including milestone payment of €14m received in January 2017

BUILDING AN INNOVATIVE AND DIFFERENTIATED PIPELINE

ERIC VIVIER

CHIEF SCIENTIFIC OFFICER

EXPERIENCE

30 YEARS IN ACADEMIC RESEARCH - IMMUNOLOGY

- D.V.M, PhD (Paris XI)
- Harvard Medical School

- Centre d'Immunologie de Marseille-Luminy

- Scripps, Rockefeller, WEHI

- European Research Council Laureate – Highly cited researcher

EXPERIENCE

30 YEARS IN ACADEMIC RESEARCH - IMMUNOLOGY

MISSION

- Translating science into survival
- Finding new targets, new formats
- Identifying mechanisms of action

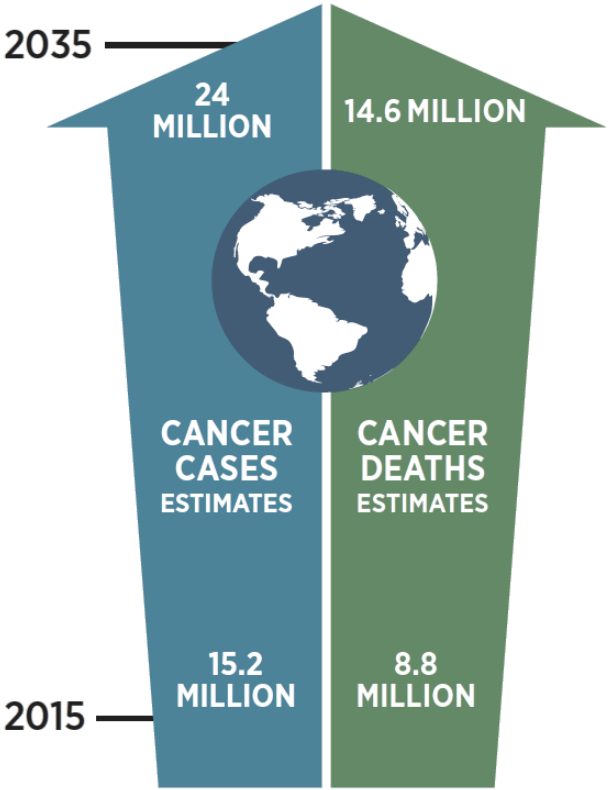
MEANS

- Expertise
- Technology
- Academic & industrial network

WHY INNATE PHARMA?

- World-class biotech company
- 4 first-in-class molecules in 15 years

CANCER: A GLOBAL CHALLENGE



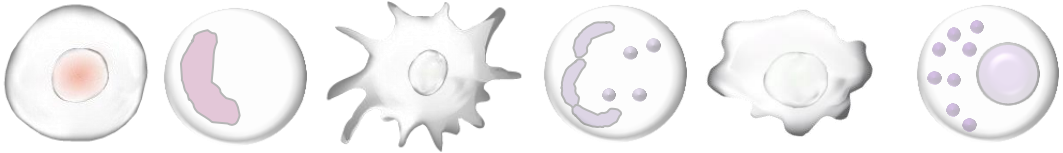
In 2005, cancer accounted for 7.5 million of the 53.6 million deaths worldwide, meaning it accounted for **1 in 7 deaths.**

In 2015, cancer accounted for 8.8 million of the 55.8 million deaths worldwide, meaning it accounted for almost **1 in 6 deaths.**

AACR Cancer Progress Report, 2017

THE IMMUNE SYSTEM

CHALLENGES
- **Microbial infections**
- **Tumors**



NK | **Innate lymphoid cells Groups 1, 2, 3** | **Dendritic cells** | **Neutrophils Eosinophils Basophils** | **Monocytes Macrophages** | **Mastocytes**

INNATE IMMUNITY

- Hours
- Whole body

EFFECTOR RESPONSE

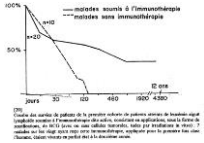
Naïve B&T cells

- Days
- From lymphoid organs

ADAPTATIVE IMMUNITY

A BRIEF HISTORY OF ANTI-TUMOR IMMUNOSURVEILLANCE

1891
New York City, USA
William Coley
'Coley toxine'



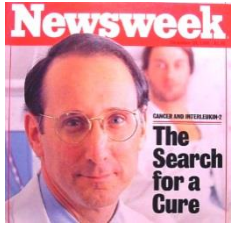
1967
Villejuif, France
Georges Mathé
BCG

1980
Bruxelles, Belgique
Thierry Boon
Tumor antigens

2001
Saint Louis, USA
Robert D. Schreiber
Tumor editing

1957
Melbourne, Australie
Sir MacFarlane Burnet
Tumor immunosurveillance

1975
Bethesda, USA,
Steven A. Rosenberg
IL-2

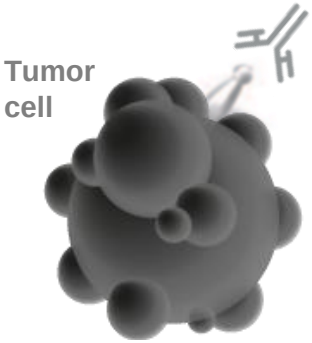


1996
Berkeley, USA
James P. Allison
CTLA-4

2002
Kyoto, Japon
Tasuku Honjo
PD-1

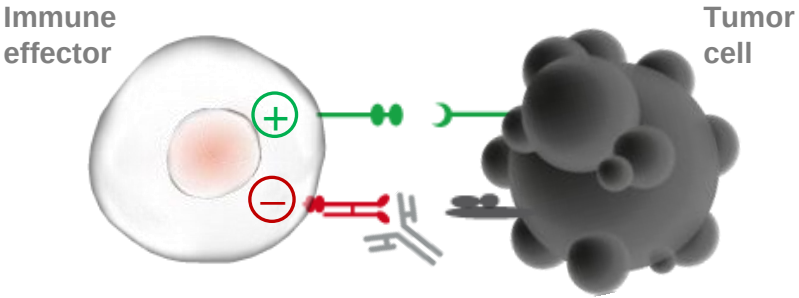
THE IMMUNO-ONCOLOGY REVOLUTION

DIRECT TARGETING OF TUMOR CELLS:
i.e. via tumor antigens



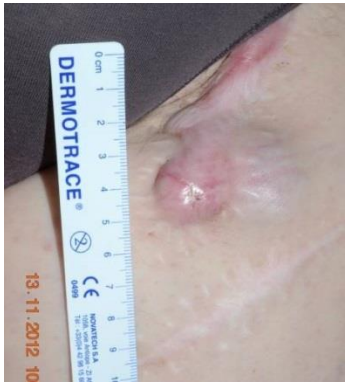
- Surgery
- Radiotherapy
- Chemotherapy

INDIRECT TARGETING OF TUMOR CELLS:
i.e. via immune checkpoints



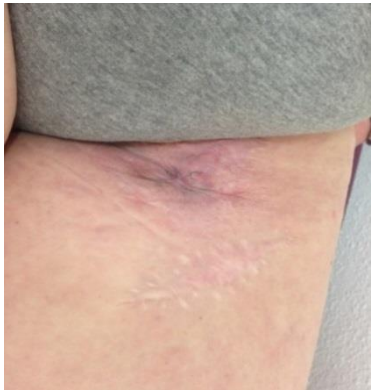
Immune
Checkpoint Inhibitors

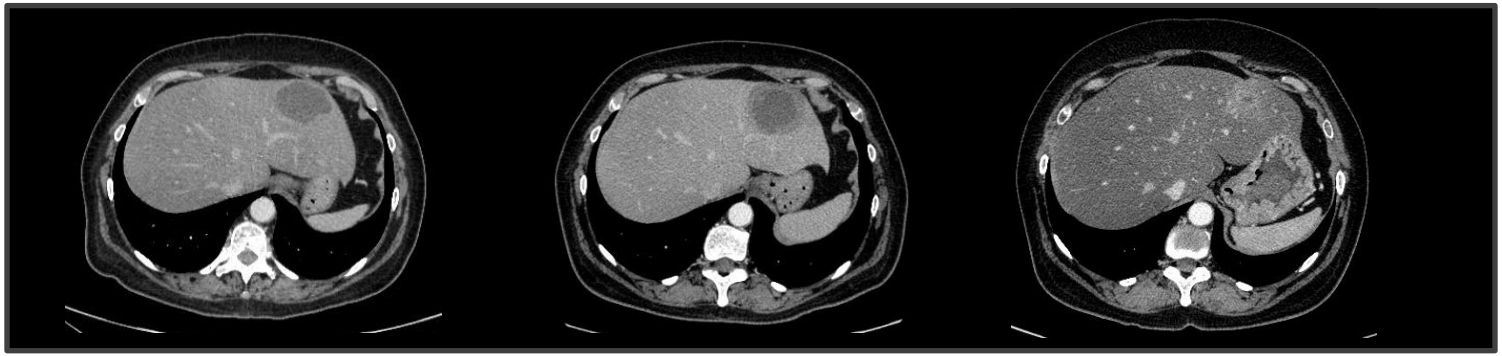
THE MAB REVOLUTION IN CANCER IMMUNOTHERAPY



Resistant to chemo

Anti-PD1 mAbs

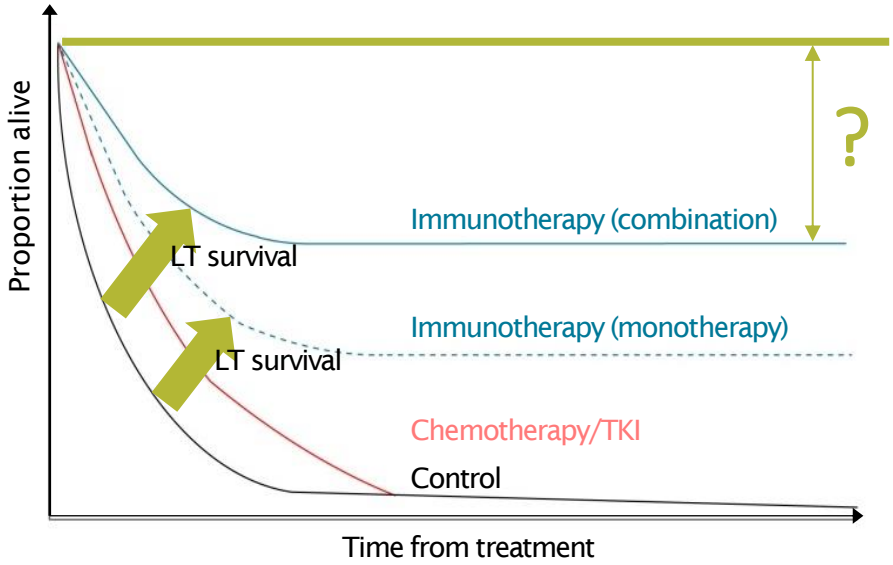




Baseline **12 weeks** **24 weeks** **52 weeks**

C. Robert, IGR

WHAT'S NEXT IN IMMUNO-ONCOLOGY?



Immune Checkpoint Inhibitors

- anti-CTLA-4
  - > Ipilimumab (**YERVOY**, BMS)
  - > Tremelimumab (MEDIMMUNE-ASTRAZENECA)
- anti-PD-1
  - > Nivolumab (**OPDIVO**, BMS/ONO)
  - > Pembrolizumab (**KEYTRUDA**, MERCK)
- anti-PD-L1
  - > Avelumab (**BAVENCIO**, MERCK KGaA/PFIZER)
  - > Durvalumab (**IMFINZI**, MEDIMMUNE-ASTRAZENECA)
  - > Atezolizumab (**TECENTRIQ**, GENENTECH/ROCHE)

WHAT'S NEXT IN IMMUNO-ONCOLOGY?

- Understand the resistance to Immune Checkpoint Inhibitors
- Increase the fraction of patients sensitive to IO treatments
- Decrease toxicity
- Identify new targets (cells and molecules)
- Identify biomarkers

WHAT'S NEXT IN IMMUNO-ONCOLOGY?

- Understand the resistance to Immune Checkpoint Inhibitors
- Increase the fraction of patients sensitive to IO treatments
- Decrease toxicity
- **Identify new targets (cells and molecules)**
- Identify biomarkers


Eye of Science/SPL
Natural-killer cells sound the alarm against cancer
nature.com

BROAD AND DIFFERENTIATED PORTFOLIO OF IO ASSETS

Target Discovery	Drug Discovery	Preclinical	Dose finding	Signal detection	Pivotal
~20 targets or concepts under exploration	Anti-Siglec-9	**IPH52** Anti-CD39	**IPH5401** Anti-C5aR	**Monalizumab** Anti-NKG2A	
	SAN-NKCE-2	**IPH53** Anti-CD73		**Lirilumab** Anti-KIR2DL1,2,3	
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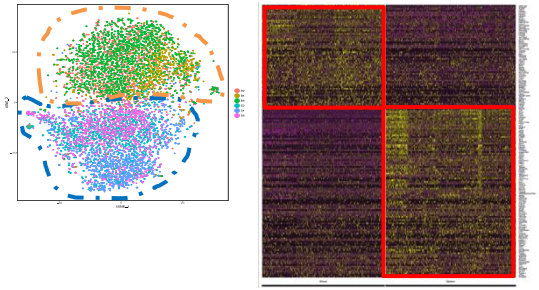
		IPH61 SAN-NKCE-1			

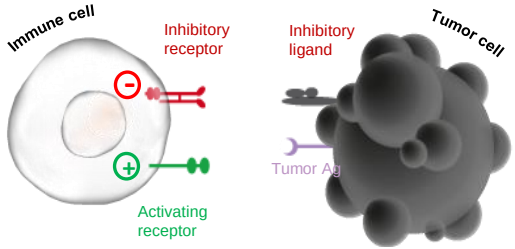
BUILDING AN INNOVATIVE AND DIFFERENTIATED PIPELINE

Human surfaceome
20,000+ genes
35,000+ proteins
7,000+ proteins that can be expressed at the cell surface
Largely unexplored



Expression: Single cell genome-wide analysis

Function: Cell-based assays



Therapy: Best/First in class Ab generation

NEXT GENERATION IO

3 STRATEGIC KEY PILLARS TO HARNESS THE POTENTIAL OF IMMUNITY

1	2	3
NK cells checkpoints (NKCP)	Tumor targeting (TAg)	Tumor Microenvironment (TME)

NEXT GENERATION IO
OUR STRATEGY

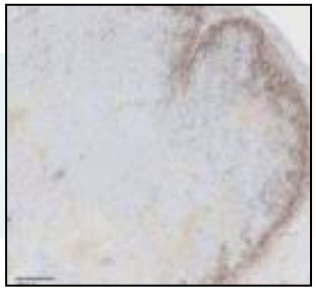
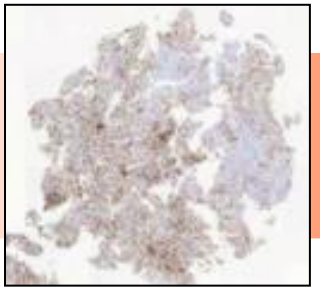
UNIQUE POSITIONNING

FIRST-IN-CLASS BEST-IN-CLASS

DIVERSIFIED APPROACH

INNATE PHARMA – PIPELINE

TARGETING DIFFERENT STATUS OF THE IMMUNE RESPONSE

No effective anti-tumor immunity	Anti-tumor immunity suppressed by TME	Sub-optimal or exhausted anti-tumor immunity
		
NK Bispecific Engagers	**IPH5401** Anti-C5aR	**Lirilumab** Anti-KIR2DL1,2,3
Antibody Drug Conjugates	**IPH53** Anti-CD73	**Monalizumab** Anti-NKG2A
	IPH52 Anti-CD39	**IPH4102** Anti-KIR3DL2
	IPH4301 Anti-MICA/B	

Noninflamed → **Inflamed**

NKCP | TAg | TME

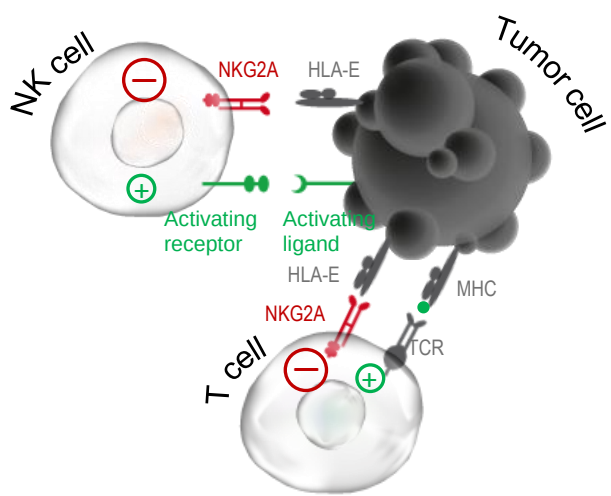
Adapted from Hedge et al., Clin Cancer Res, 2016

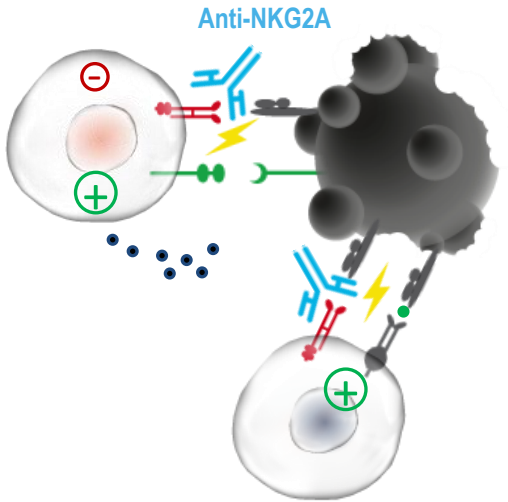
NEXT GENERATION IO
3 STRATEGIC KEY PILLARS

1	2	3
NK cells checkpoints (NKCP) **NKG2A**	**Tumor targeting (TAg)**	**Tumor Microenvironment (TME)**

ANTI-NKG2A IS A NOVEL IMMUNE CHECKPOINT INHIBITOR IN CANCER

- Monalizumab (IPH2201) is a first-in-class anti-NKG2A humanized blocking antibody

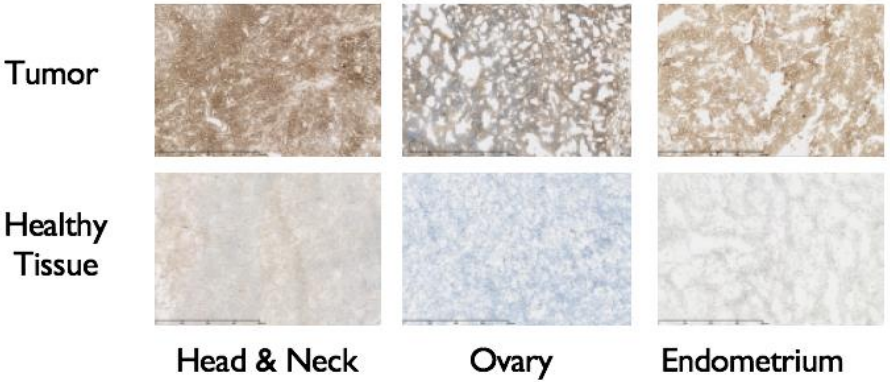




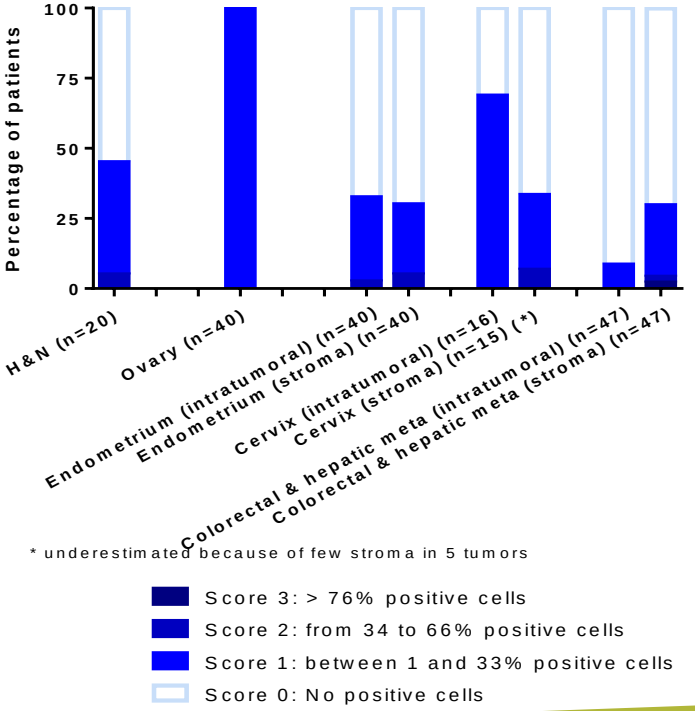
NK cell and T cell inhibition by NKG2A + **Activation by NKG2A blockade**

NKG2A / HLA-E PATHWAY IS UPREGULATED IN TUMORS

HLA-E on tumor cells

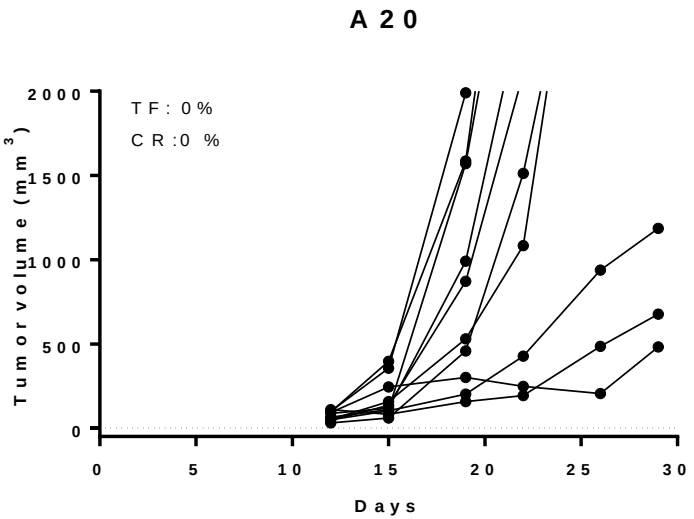


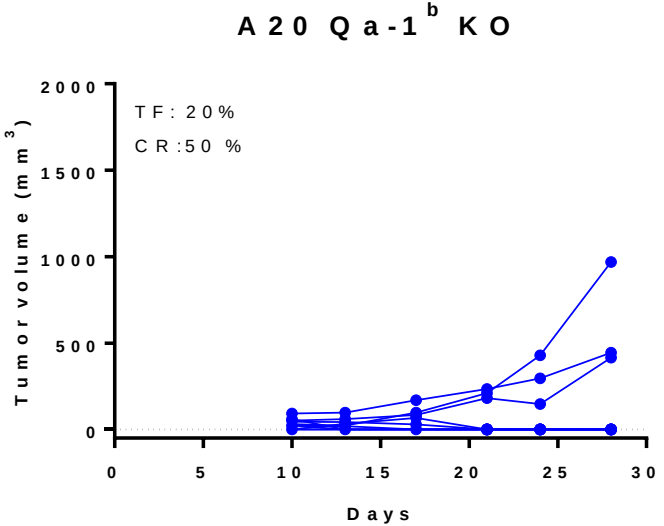
NKG2A on TILs



André et al. unpublished

NKG2A/Q_A-1^b CONTROL TUMOR GROWTH



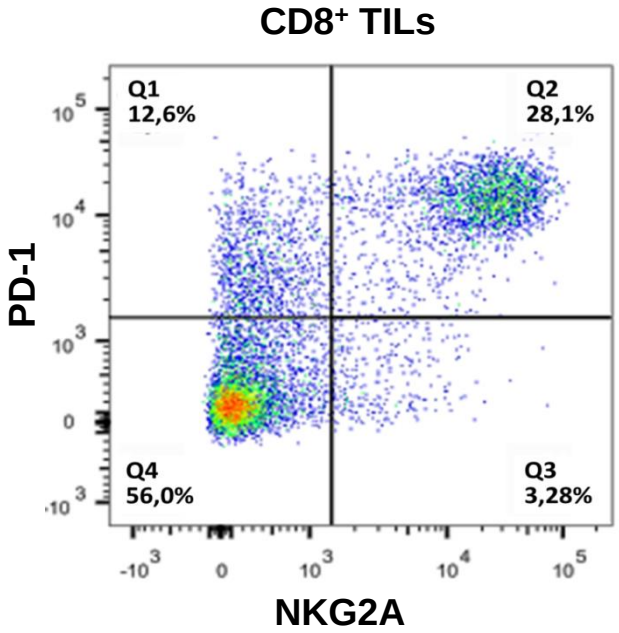


Individual A20 and A20 Qa-1^b KO and A20 PD-L1 KO tumor growth after sub-cutaneous engraftment of 5x10^6 A20 tumor cells (n=10) in BALB/C mice.

TF: Tumor Free, CR: Complete Regression

André et al. unpublished

PD-1^{HIGH} CD8^{+} TILS CO-EXPRESS NKG2A

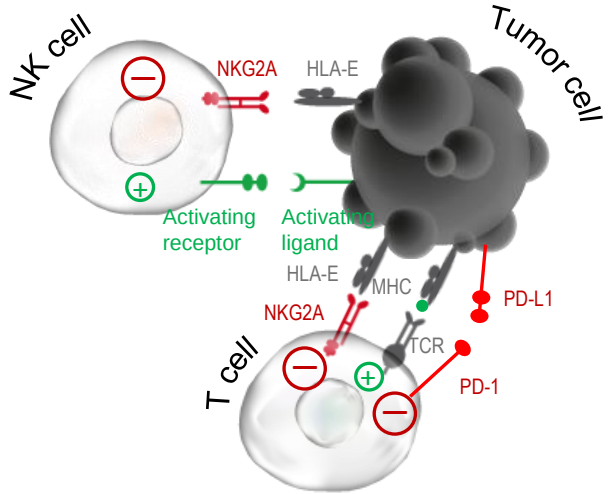


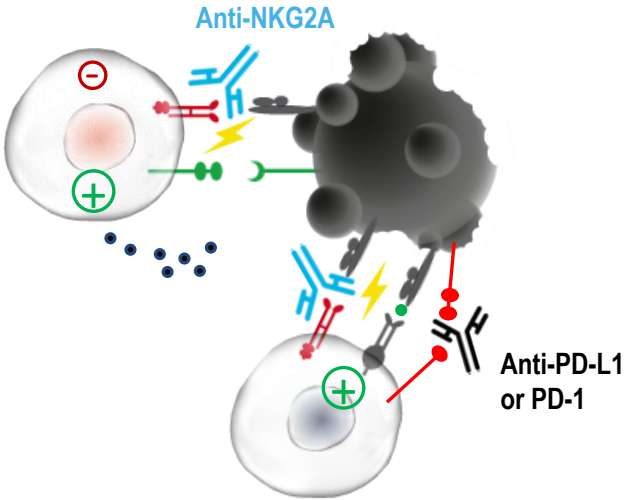
Expression of NKG2A and PD-1 on isolated CD8^{+} TILs (day 20)

A20 B cell lymphoma into BALB/C mice

André et al. unpublished

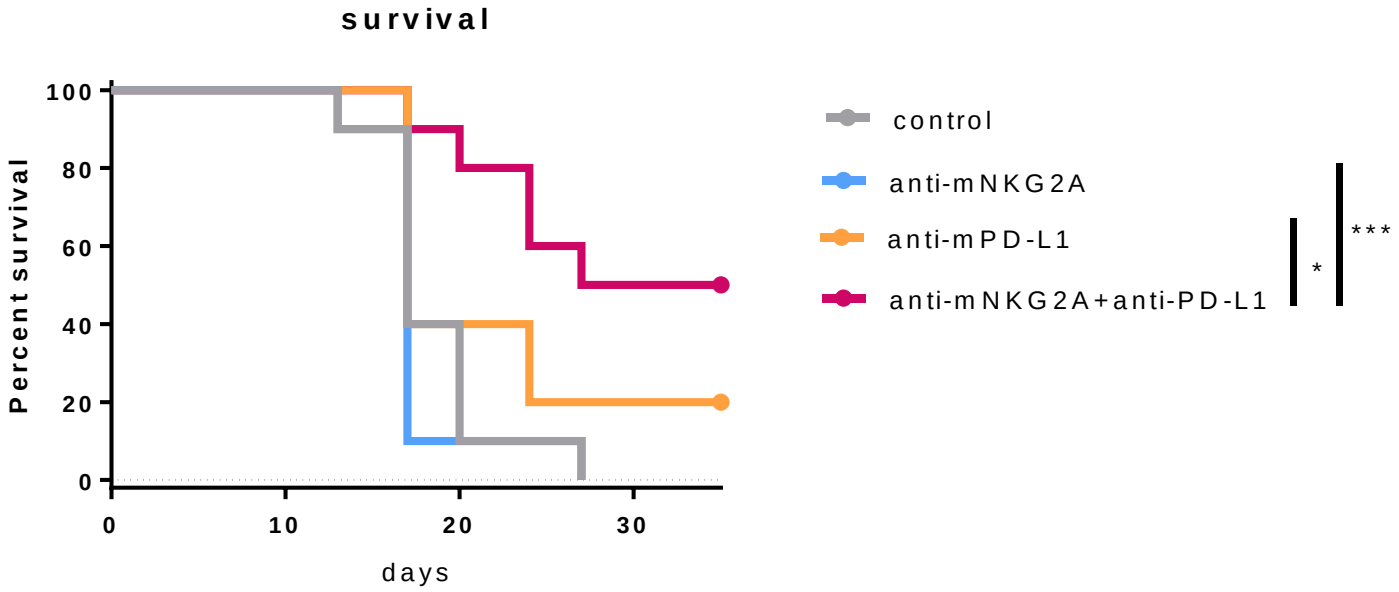
NKG2A AND PD-L1 BLOCKADES ARE COMPLEMENTARY





NK cell and T cell inhibition by NKG2A + **Activation by NKG2A blockade**

NKG2A BLOCKADE INCREASES PD-L1 ANTI-TUMORAL EFFICACY

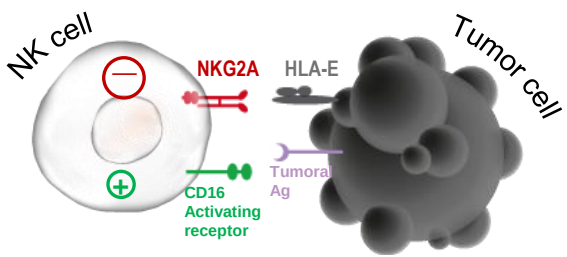


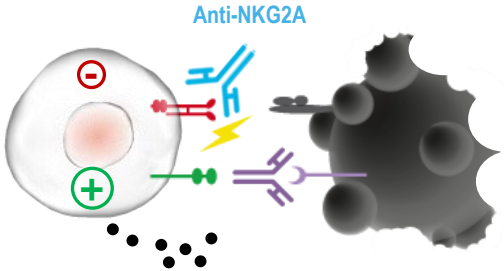
RMA-Rae1 into B6 mice

P=0.03 (*), P=0.0006 (***), Grehan-Breslow-Wilcoxon test

André et al. unpublished

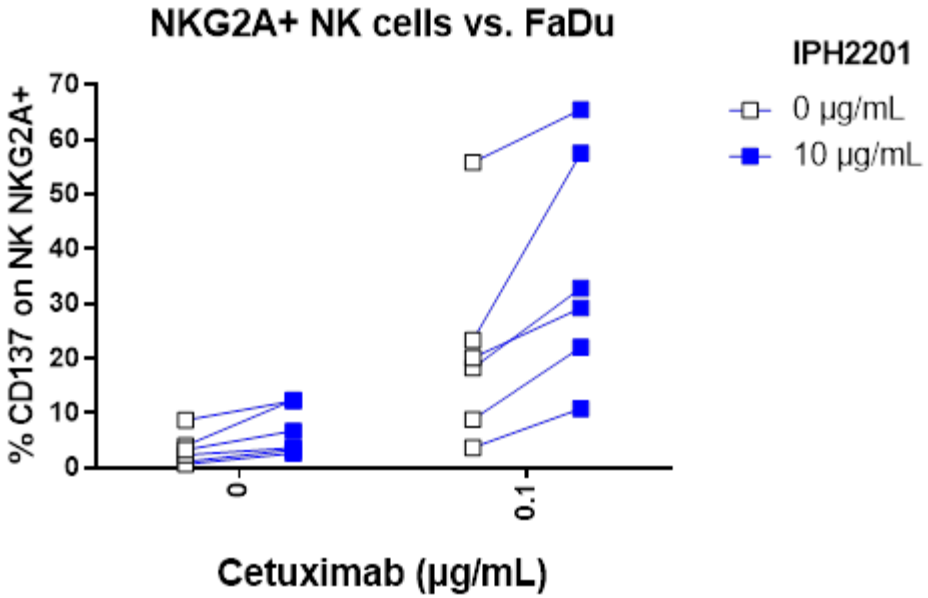
NKG2A BLOCKADE ENHANCES ADCC IN A HLA-E^{+} CONTEXT





NK cell inhibition by NKG2A + **ADCC enhancement by NKG2A blockade**

NKG2A BLOCKADE ENHANCES CETUXIMAB-INDUCED ADCC OF H&N TUMOR CELLS



NEXT GENERATION IO
3 STRATEGIC KEY PILLARS

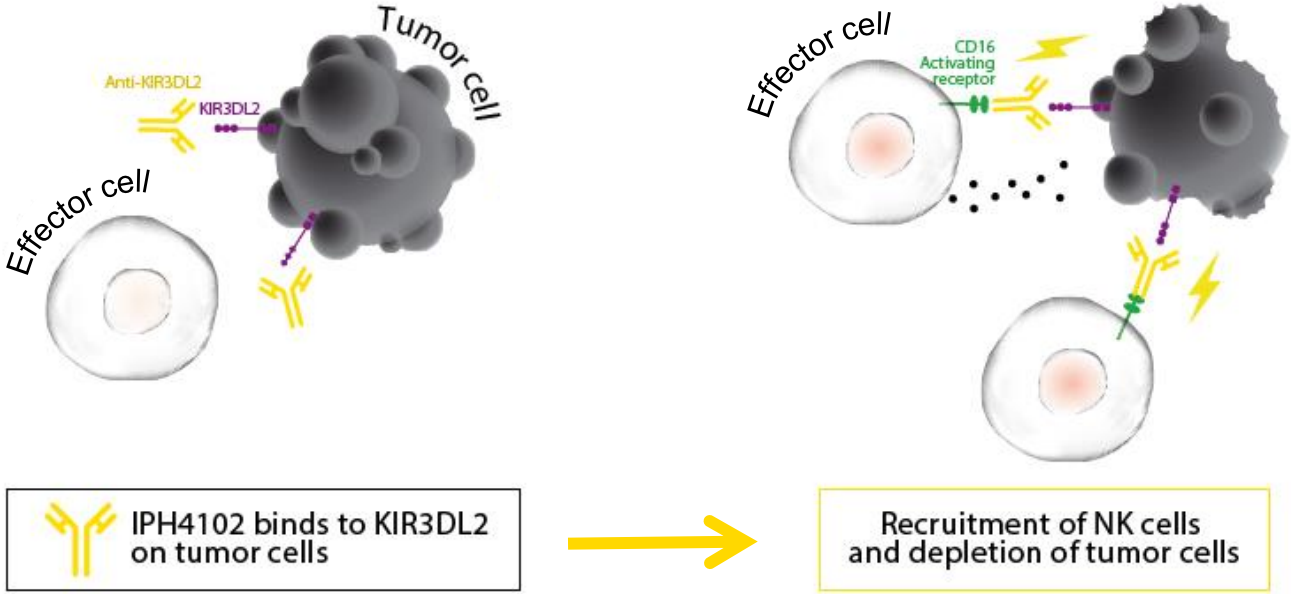
1	2	3
NK cells checkpoints (NKCP)	**Tumor targeting (TAg)** **KIR3DL2** **MICA/B** **NKp46 NKCE**	**Tumor Microenvironment (TME)**

NEXT GENERATION IO
3 STRATEGIC KEY PILLARS

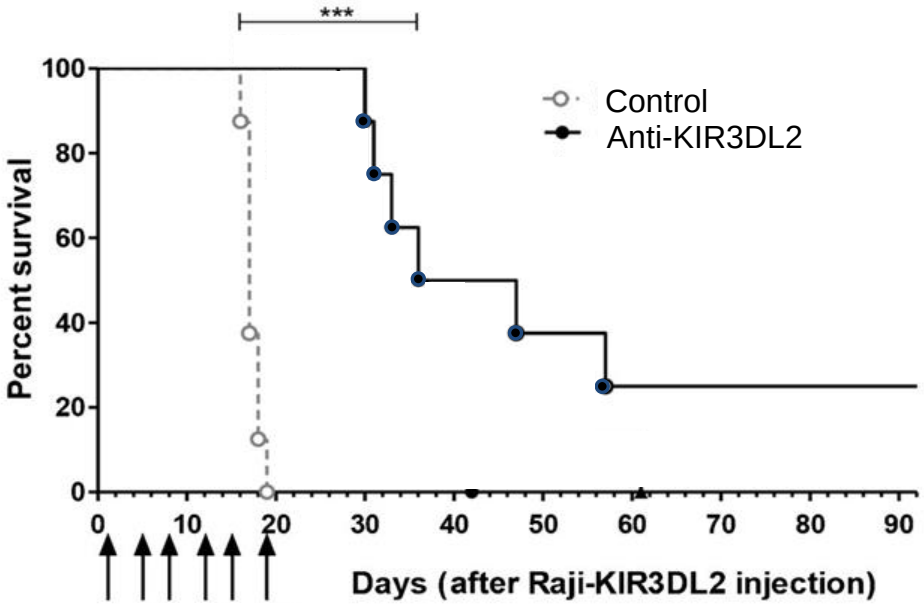
1	2	3
NK cells checkpoints (NKCP)	**Tumor targeting (TAg)** **KIR3DL2** **MICA/B** **NKp46 NKCE**	**Tumor Microenvironment (TME)**

KIR3DL2 IS A TUMOR SPECIFIC ANTIGEN IN CTCL

- IPH4102 is a first-in-class anti-KIR3DL2 humanized cytotoxicity-inducing antibody



KIR3DL2 TARGETING INDUCES ANTI-TUMORAL EFFICACY

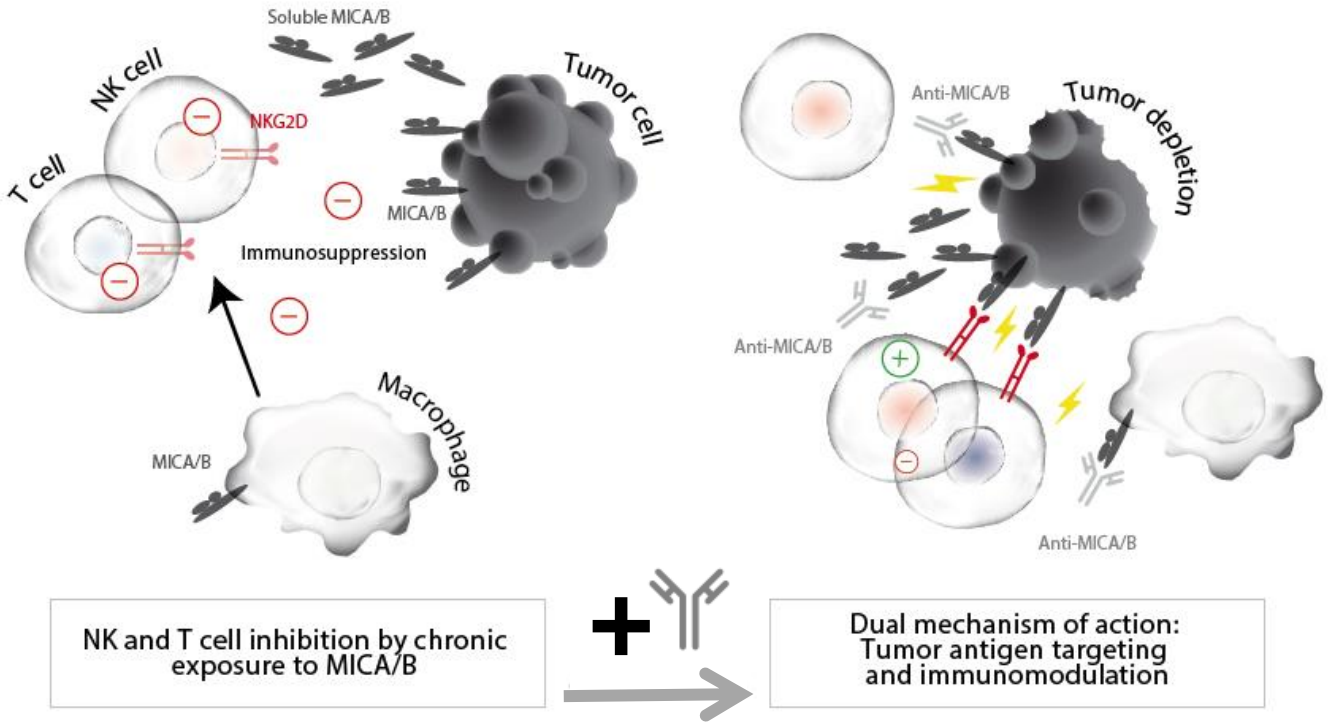


Marie-Cardine et al, Cancer Res 2014

NEXT GENERATION IO
3 STRATEGIC KEY PILLARS

1	2	3
NK cells checkpoints (NKCP)	**Tumor targeting (TAg)** **KIR3DL2** **MICA/B** **NKp46 NKCE**	**Tumor Microenvironment (TME)**

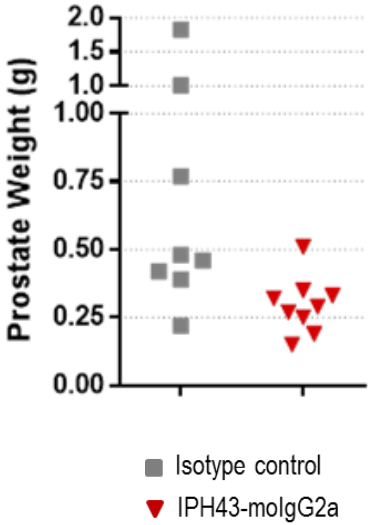
MICA/B IS INDUCED ON TUMOR CELLS AND DOWNREGULATES NKG2D

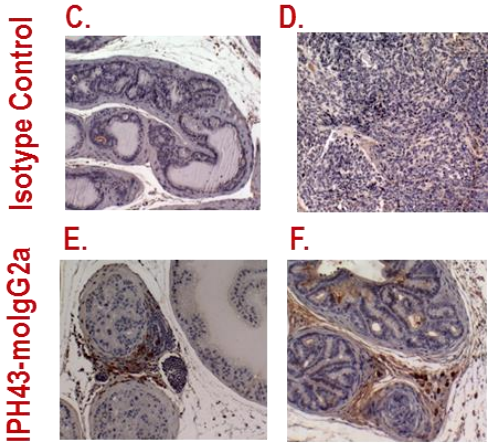


MICA/B CAN BE TARGETED BY NAKED AB OR ADC

Anti-MICA naked Ab

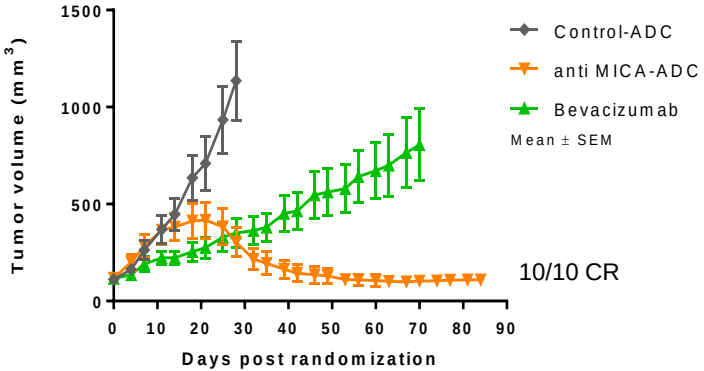
TRAMP-MICB tumor model





Anti-MICA-ADC

PDX (human breast)



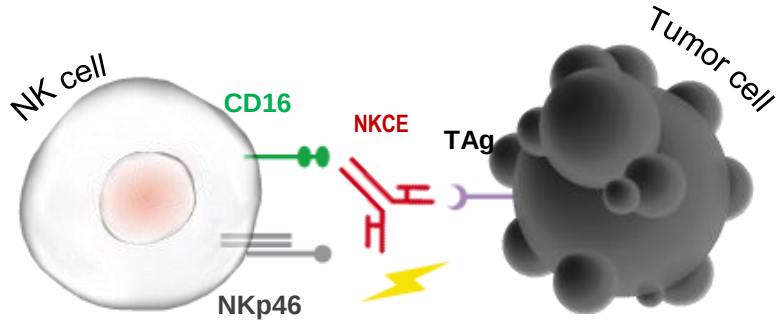
10/10 CR

NEXT GENERATION IO
3 STRATEGIC KEY PILLARS

1	2	3
NK cells checkpoints (NKCP)	**Tumor targeting (TAg)** **KIR3DL2** **MICA/B** **NKp46 NKCE**	**Tumor Microenvironment (TME)**

NK CELL ENGAGER (NKCE) MULTISPECIFIC ANTIBODY TECHNOLOGY

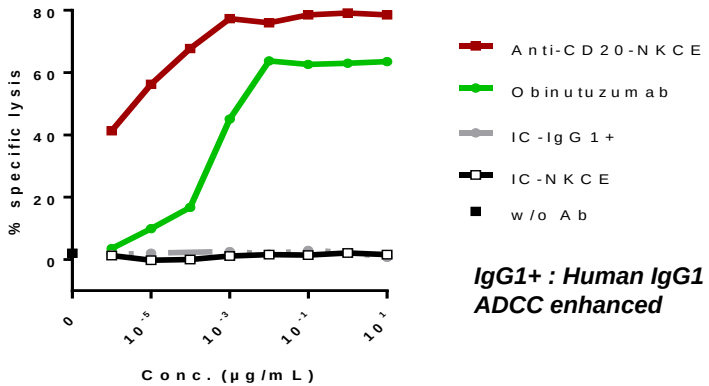
- NKp46-NKCE binds to
  - > an antigen at the surface of tumor cells
  - > NKp46 activating receptor on NK cells and CD16 (FcγRIII)
- NKp46-NKCE may reduce the risk of side-effects associated with T cell engagers
- Library of proprietary anti-NKp46 mAbs and multispecific formats with PK and CMC advantages
- Opportunity for internal discovery NKCE targets as well as through collaboration



This project has been financially supported by the European Union by means of the European Regional Development Fund.

ANTI-CD20-NKP46-NKCE INDUCES ANTI-TUMORAL EFFICACY

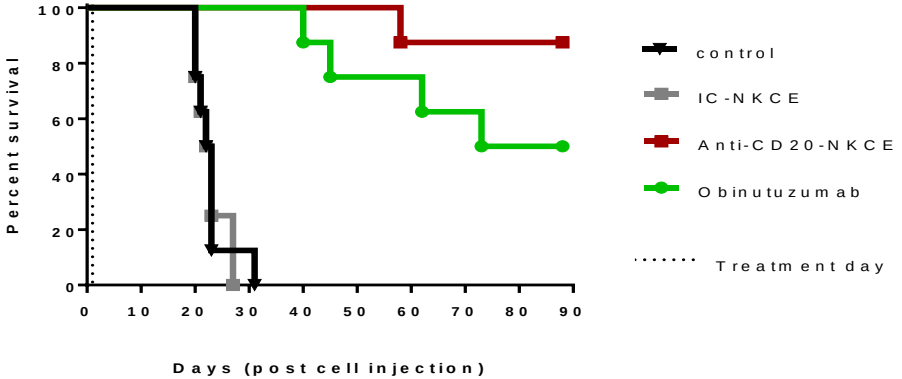
In vitro



IgG1+ : Human IgG1 ADCC enhanced

51Cr release assay / Resting NK cells vs Daudi

In vivo



CB17 SCID mice engrafted IV with Raji cells (5.10^6) and treated at day1 with 1µg of compound.

NEXT GENERATION IO
3 STRATEGIC KEY PILLARS

1	2	3
NK cells checkpoints (NKCP)	**Tumor targeting (TAg)**	**Tumor Microenvironment (TME)** **Adenosine pathway** **MDSC**

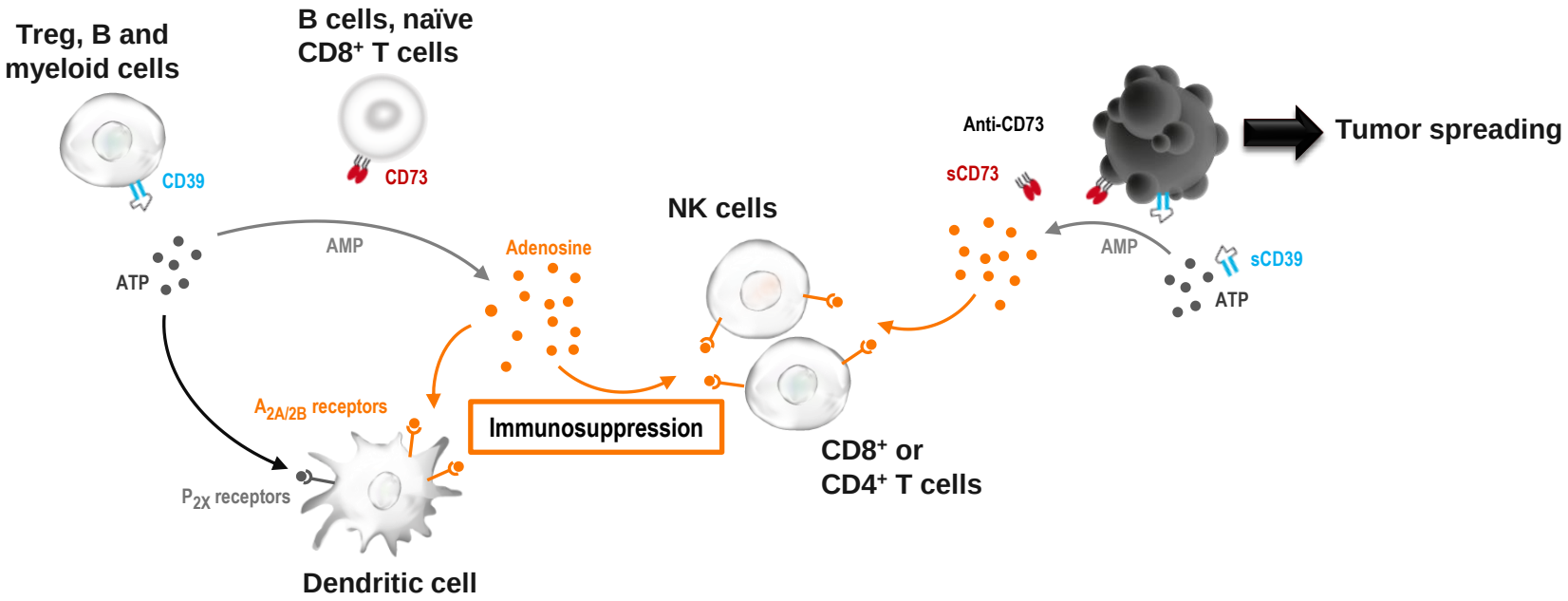
Tumor microenvironment

NEXT GENERATION IO
3 STRATEGIC KEY PILLARS

1	2	3
NK cells checkpoints (NKCP)	**Tumor targeting (TAg)**	**Tumor Microenvironment (TME)** **Adenosine pathway** **MDSC**

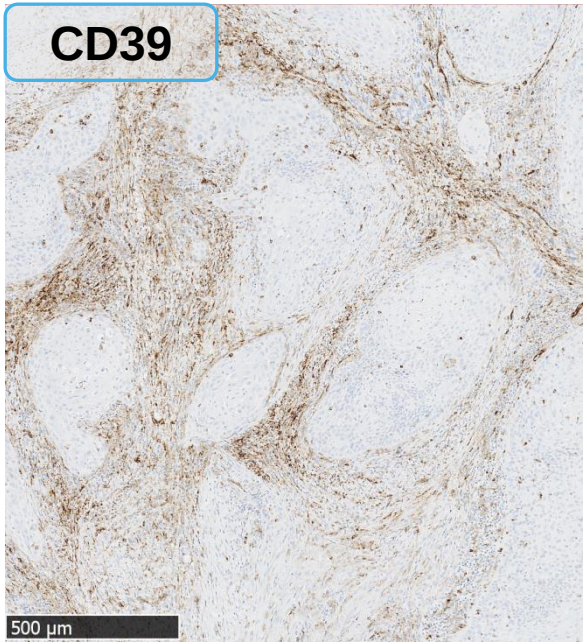
Tumor microenvironment

ADENOSINE PATHWAY IS IMMUNOSUPPRESSIVE IN THE TME



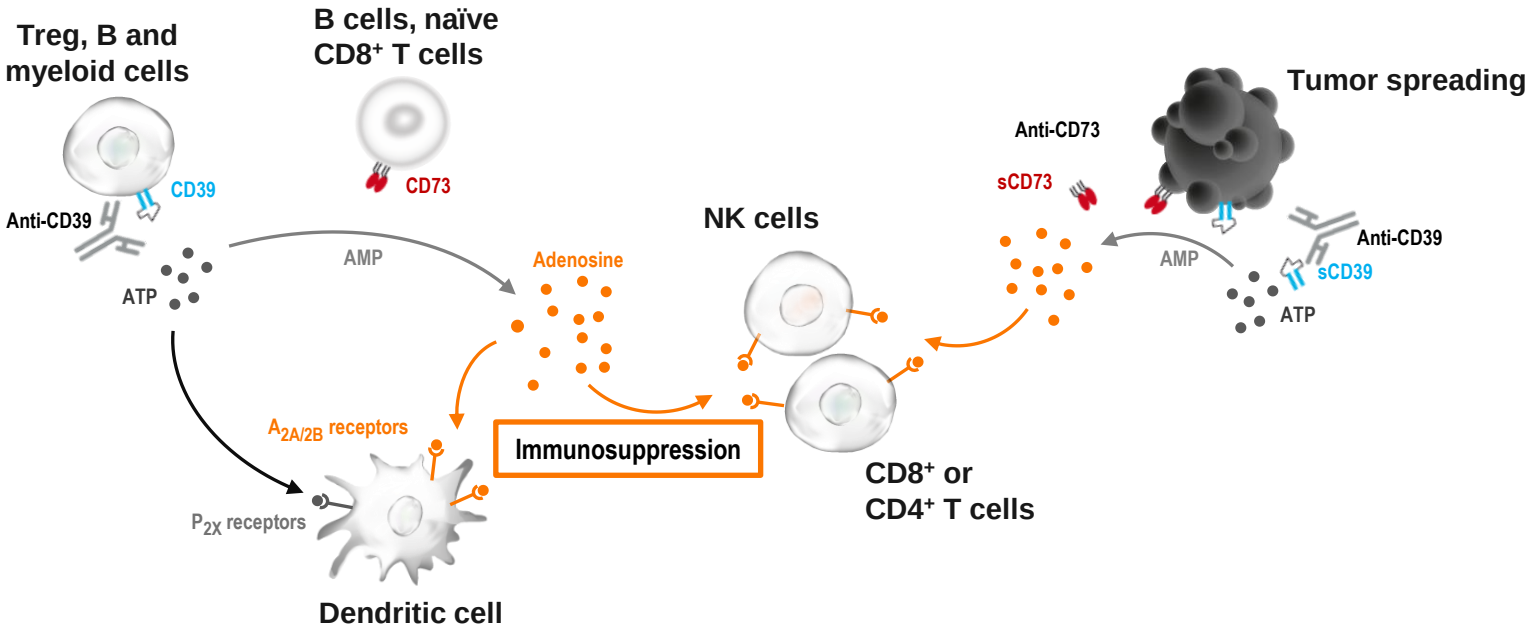
ATP : *adenosine triphosphate* ***AMP :*** *adenosine monophosphate*

CD39 EXPRESSION IN HEAD AND NECK TUMORS



CD39 is expressed on TILs and vascular endothelial cells

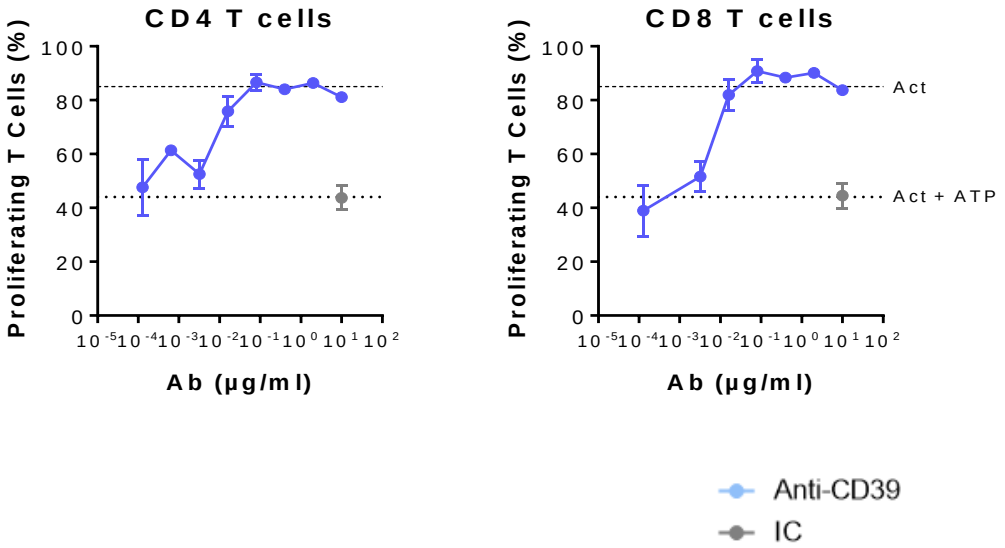
CD39 BLOCKADE INHIBITS BOTH ATP DEGRADATION AND ADENOSINE GENERATION



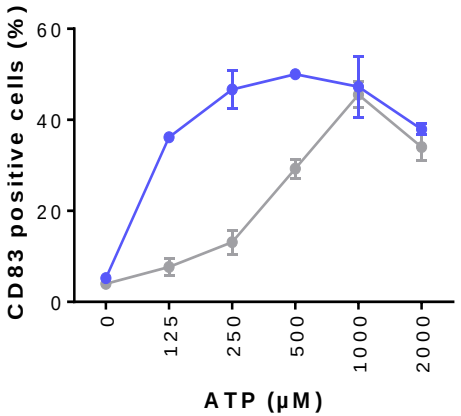
ATP : *adenosine triphosphate* ***AMP :*** *adenosine monophosphate*

LEAD ANTI-CD39 AB RESTORES IMMUNE RESPONSE IN THE PRESENCE OF ATP

T cell proliferation assay

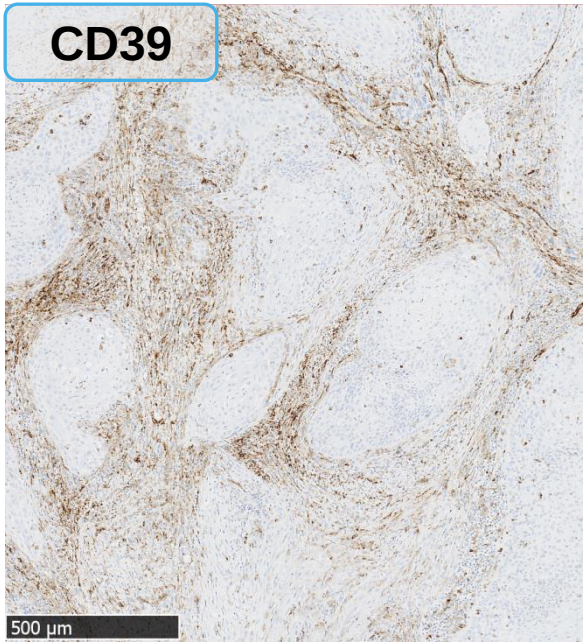


DC activation

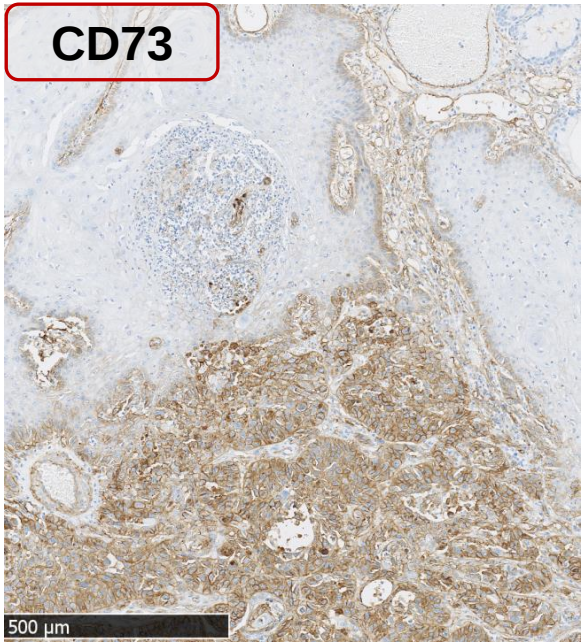


Tumor microenvironment

CD39 AND CD73 EXPRESSION IN HEAD AND NECK TUMORS

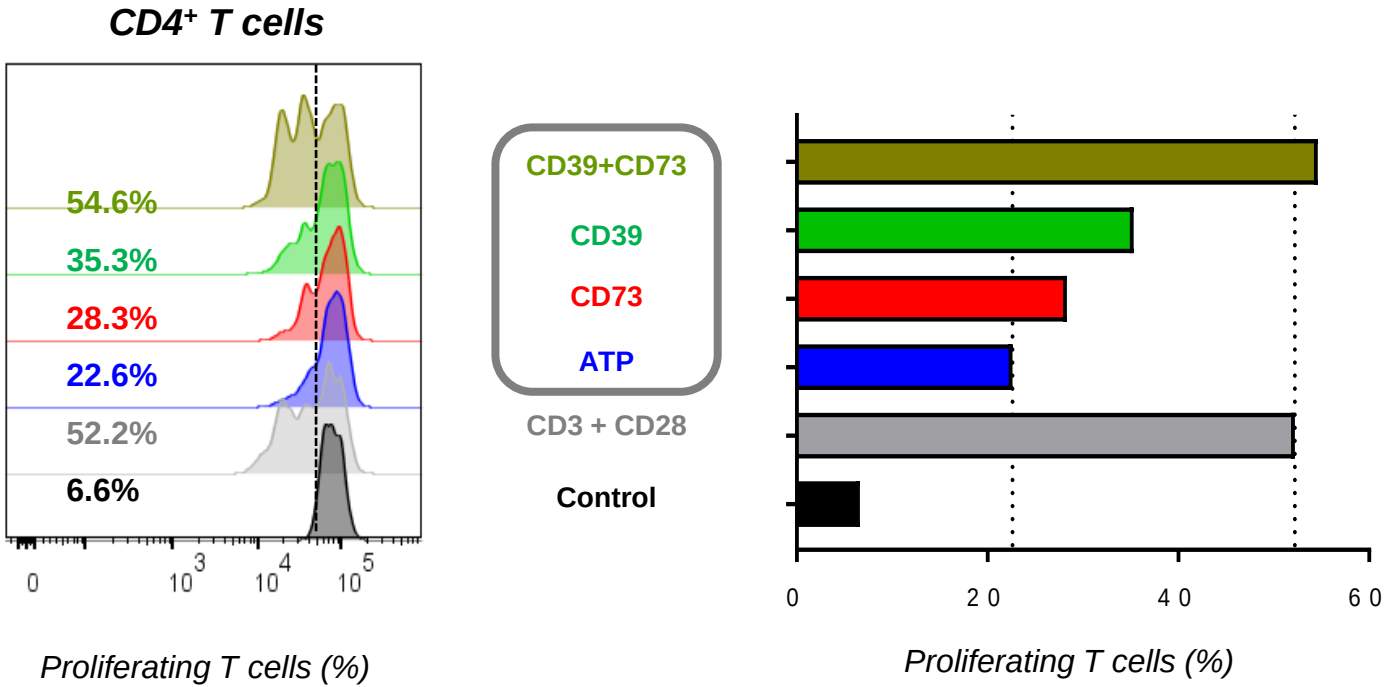


CD39 is expressed on TILs and vascular endothelial cells

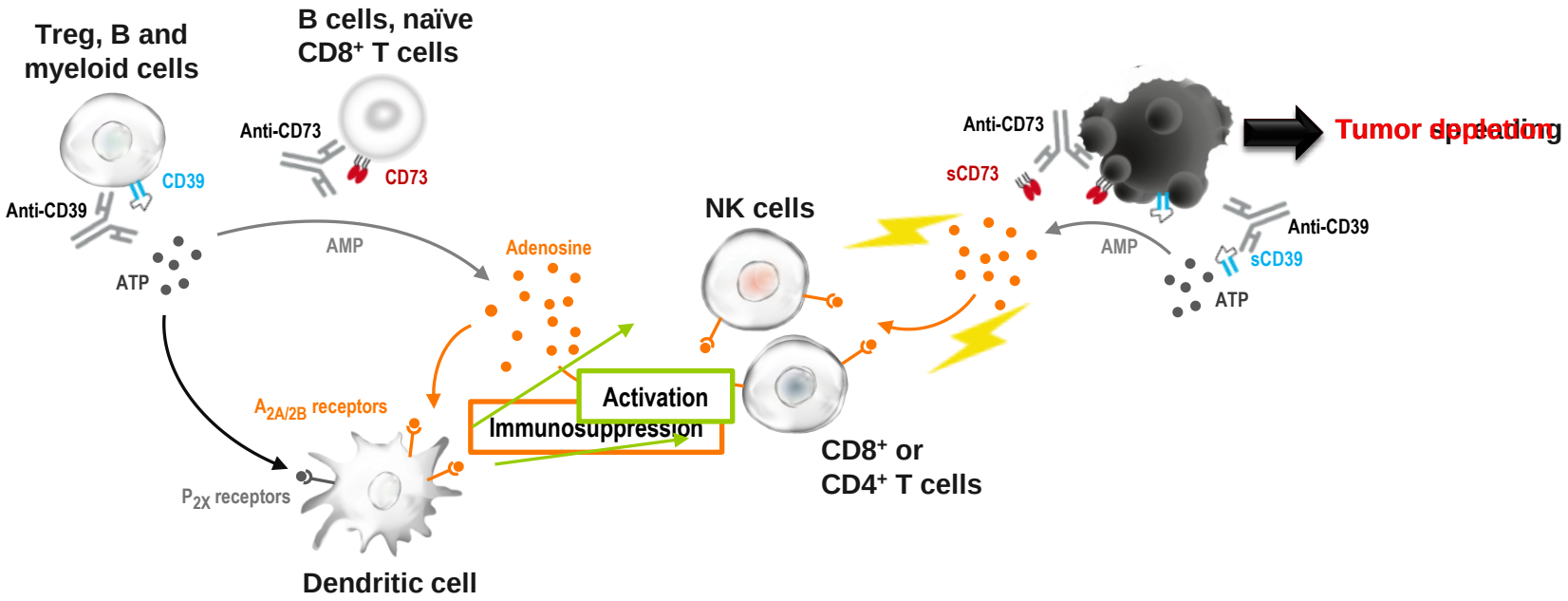


CD73 is expressed on tumor cells, TILs and vascular endothelial cells

CD39/CD73 BLOCKADE SYNERGIZE TO REVERSE ATP-MEDIATED T CELL SUPPRESSION



CD39/CD73 BLOCKADE AIMS AT REVERSING IMMUNOSUPPRESSION IN THE TME



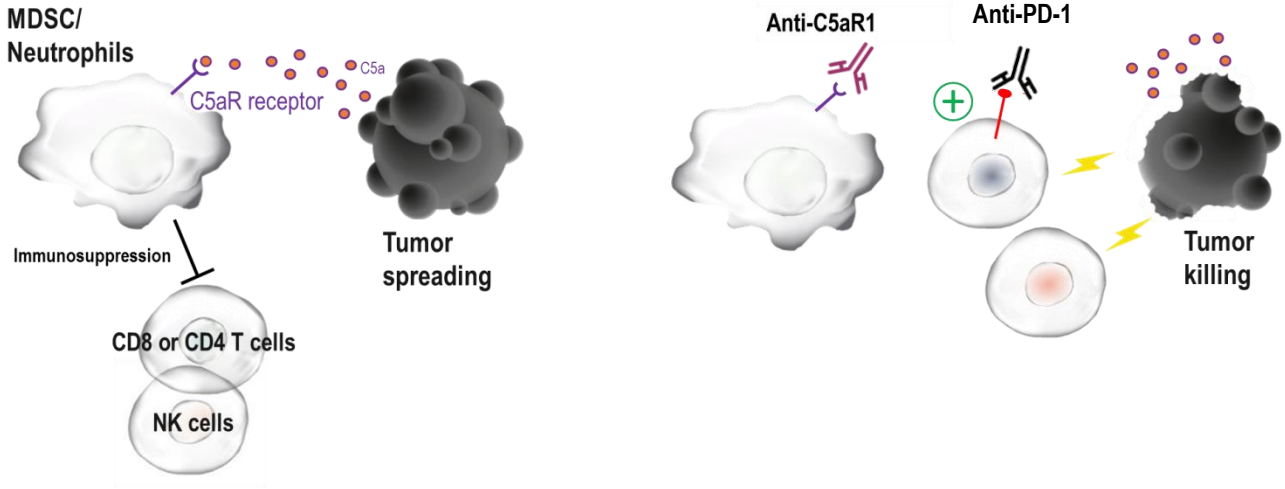
ATP : *adenosine triphosphate* ***AMP :*** *adenosine monophosphate*

NEXT GENERATION IO
3 STRATEGIC KEY PILLARS

1	2	3
NK cells checkpoints (NKCP)	**Tumor targeting (TAg)**	**Tumor Microenvironment (TME)** **Adenosine pathway** **MDSC**

Tumor microenvironment

C5AR BLOCKADE INHIBITS MDSC/NEUTROPHIL RECRUITMENT AND ACTIVATION IN THE TME

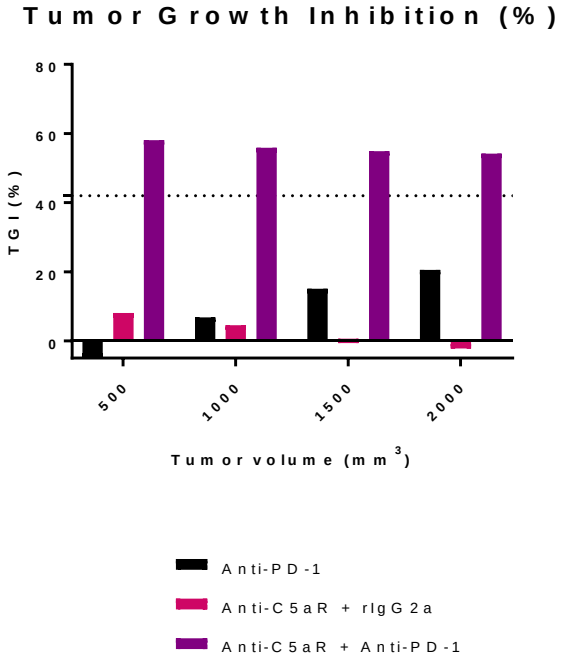


MDSC mediate pro-tumoral inflammation and immune suppression

+

C5aR blockade decreases MDSC infiltration and their immunosuppression of effector cells

C5AR/PD-1 BLOCKADE INDUCES TUMOR GROWTH INHIBITION IN A PD-1 RESISTANT MODEL



Fares et al. ICI 2017

Tumor microenvironment

BROAD AND DIFFERENTIATED PORTFOLIO OF IO ASSETS

Target Discovery	Drug Discovery	Preclinical	Dose finding	Signal detection	Pivotal
~20 targets or concepts under exploration	Anti-Siglec-9	**IPH52** Anti-CD39	**IPH5401** Anti-C5aR	**Monalizumab** Anti-NKG2A	
	SAN-NKCE-2	**IPH53** Anti-CD73		**Lirilumab** Anti-KIR2DL1,2,3	
	Other undisclosed targets	**IPH4301** Anti-MICA/B		**IPH4102** Anti-KIR3DL2	
		IPH61 SAN-NKCE-1			

Tumor microenvironment

THINK

BE CREATIVE

PROVIDE SOLUTIONS

OPENING

PROPRIETARY PORTFOLIO

PIERRE DODION

CHIEF MEDICAL OFFICER

NEXT GENERATION IO
3 STRATEGIC KEY PILLARS

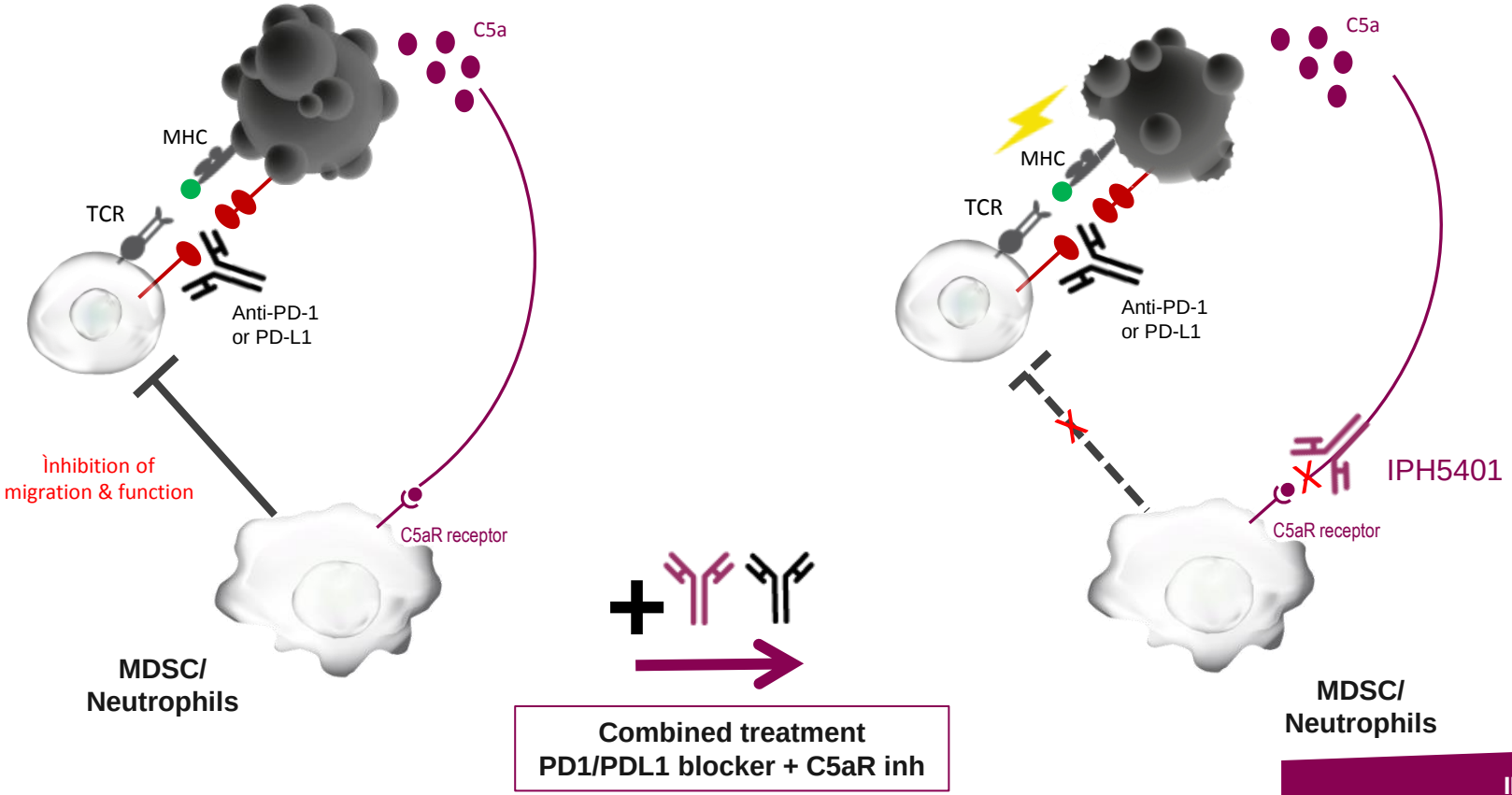
1	2	3
NK cells checkpoints (NKCP)	**Tumor targeting (TAg)**	**Tumor Microenvironment (TME)** **IPH5401** (target: C5aR)

WHAT IS IPH5401?

- C5aR inhibitor: monoclonal antibody targeting the receptor (C5aR) to C5a
- C5a results from the cleavage of C5 as part of the complement cascade
- C5a stimulates the recruitment and functional activation of myeloid derived suppressor cells (MDSCs) and regulatory T-cells (Tregs)
  - > Leads to the inhibition of immune effector cells
- Inhibition of C5aR signaling was shown to increase CD8 T cell infiltration and function

MECHANISM OF ACTION IPH5401

ADDING A C5AR INHIBITOR RESTORES THE EFFICACY OF PD1/PDL1 BLOCKERS



IPH5401: PHASE 1 SAFETY, PHARMACOKINETIC AND PHARMACODYNAMIC DATA

Favorable safety profile in single & multi-dose, placebo controlled phase 1 trials in RA[1]

	Single dose	Multiple dose
Dose range (mg/kg)	0.02-10 (iv) 0.2-4 (sc)	0.25-4 (sc)
Nr of pts (IPH5401/placebo)	27 / 9	18 / 6
% pts with AE (IPH5401/placebo) [2]	67 / 44	78 / 50
Related AEs	3	4
RX discontinuation	0	0
Pts with anti drug antibodies	4 (0 neutralizing)	0
Full receptor occupancy	4.3 wks (10 mg/kg iv) 1.8 wks (4 mg/kg sc)	90% occupancy at 1-4 mg/kg Dose related duration

[1] RA: rheumatoid arthritis [2] Most frequent AEs: nasopharyngitis, headache

PRIORITIZED INDICATIONS BASED ON C5AR EXPRESSION[1]

Tumor type [1]	C5aR expression	Impact on prognosis
NSCLC	**80%**	**Poor prognosis**
UCC	73%	Poor prognosis
HCC	**68%**	**Not known**
CRC	60%	Not known
RCC	61%	Not known
Gastric cancer	30-35%	Poor prognosis
Prostate cancer	35%	Poor prognosis
Breast cancer TNBC	13% 27%	Poor prognosis

[1] Gu J et al. Lung Cancer 2013; 81:259-265. Hu W et al. Exp Mol Pathol 2016;100:101-8. Idorn M et al. Cancer Immunol Immunother 2014; 63:1177–87. Imamura T et al, Breast Cancer 2016; 23:876–85. Kaida T et al, Oncotarget, 2016;51:84798-809. Maeda Y et al, Oncol Rep 2015;33:1844-50. Nitta, H et al. Clin Cancer Res 2013; 19: 2004-13. Nitta H et al, Med Oncol 2016;33:118-27. Wada Y et al, Oncol Lett 2016; 12: 3995-4000

C5AR EXPRESSION NEGATIVELY IMPACTS LONG TERM OUTCOME IN NSCLC

C5aR expression impact on long term outcome in 208 previously untreated NSCLC

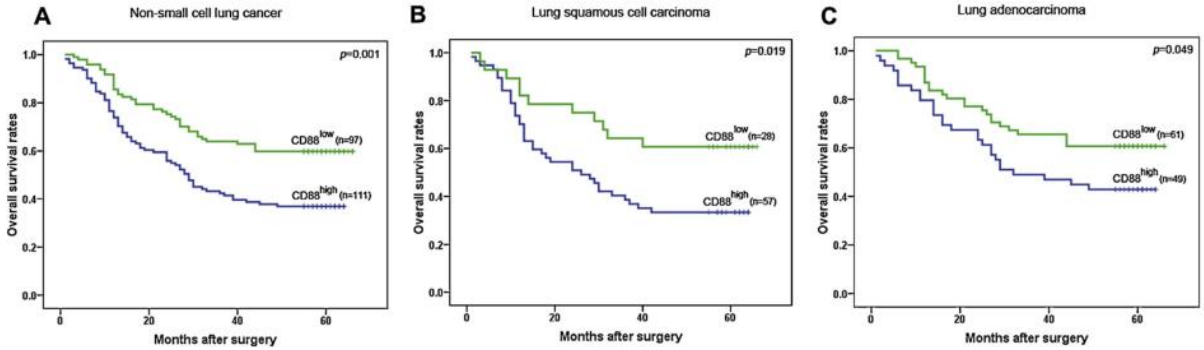
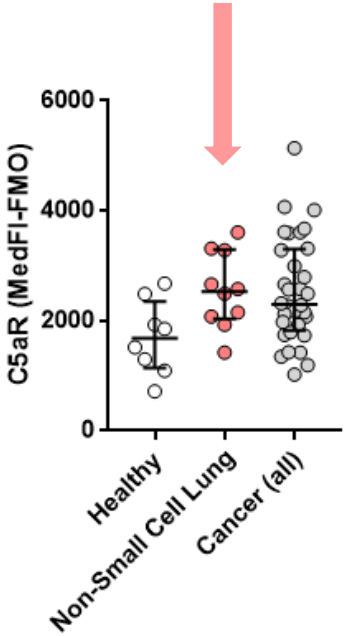


Fig. 3. Prognostic significance assessed by Kaplan–Meier survival estimates and log-rank tests. Comparisons of OS by CD88 expression in NSCLC (A), lung squamous cell carcinoma (B), and lung adenocarcinoma (C).

- The 5-year OS was significantly lower in high expressors of C5aR than in low expressors (p = 0.001)
- In a multivariate analysis, C5aR expression was an independent prognostic factor for patients' OS (HR = 1.614, 95% CI 1.082–2.407, p = 0.019)

An increase in C5aR expression by neutrophils is seen in NSCLC

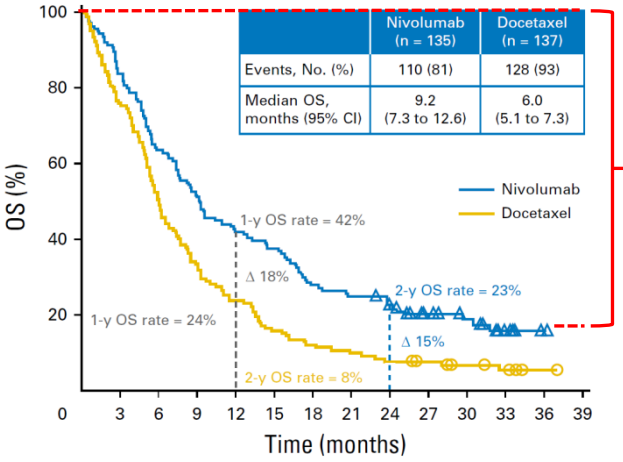


Data on file, Innate. Gu et al, 2013

PRIORITIZED INDICATIONS BASED ON MEDICAL NEED AND POTENTIALLY ACCELERATED PATH TO MARKET

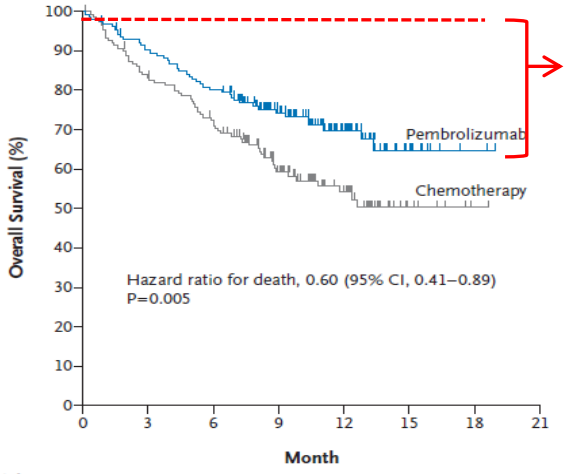
Tumor type	Description of unmet medical need
NSCLC	• second line, post platinum: rate of long term failure as high as 80%: • first line: rate of long term failure of 30%
HCC	

272 pts with squamous histology, 2nd line setting
(Checkmate trials 017 & 57, 2yrs FU)



80% long term failure rate

Pembrolizumab vs chemotherapy in patients with
> 50% PDL1 expression (Keynote 024 trial)



30% long term failure rate

Reck et al, 2016. Corey et al, 2016. Horn et al, 2017. FDA website

PRIORITIZED INDICATIONS BASED ON MEDICAL NEED AND POTENTIALLY ACCELERATED PATH TO MARKET

Tumor type	Description of unmet medical need
NSCLC	• second line, post platinum: rate of long term failure as high as 80%: • first line: rate of long term failure of 30%
HCC	• second line post sorafenib

- Sorafenib: first targeted therapy to demonstrate activity in HCC
  - > ~ 3 months gain in OS; substantial toxicity
- Regorafenib:
  - > Again limited OS gain

- Nivolumab: phase 2 study in 262 sorafenib-pretreated patients
  - > 15% ORR; median duration of 17 months and median OS of 15 months
  - > 75% OS at 9 months
  - > Approved by FDA in 2017; withdrawn from EMA review
- Overall, HCC remains an unmet medical need – opportunity to augment the activity seen with nivolumab

Llovet et al, 2008. Bruix et al, 2016. Cheng et al, 2018. Khouery et al, 2017

ASTRAZENECA COLLABORATION TO ACCELERATE PROOF-OF-CONCEPT IN NSCLC AND HCC

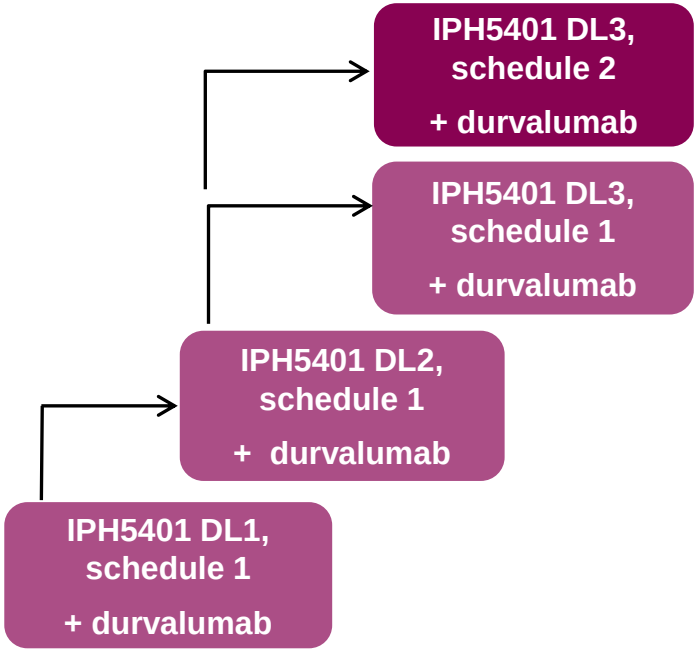
	AstraZeneca/MedImmune Collaboration
Type of collaboration	Clinical agreement (access to drug, 50% trial cost sharing)
Tumor type for expansion cohorts	NSCLC 2^{ary} resistance (IO pretreated) IO naive HCC = unmet medical needs
PD1/PDL1 blockers sensitivity	Low
Partner drug	Durvalumab
Study design	Dose escalation Cohort expansion
Study start	2H18

SMART DEVELOPMENT PROGRAM WITH LIMITED DOSE-ESCALATING PART

- In combination with durvalumab
- Very limited dose escalation part
- Cohort expansion(s) at recommended phase 2 dose/schedule
- Indications selection: NSCLC, HCC
- Extensive PK/PD exploration (e.g. C5aR, C5a, MDSCs, CD8, PDL1, cytokines, TMB)

COMBINATION IPH5401 + DURVALUMAB
PROPOSED STUDY DESIGN

Dose escalation part: 3+3 model
primary endpoint: safety, RP2D

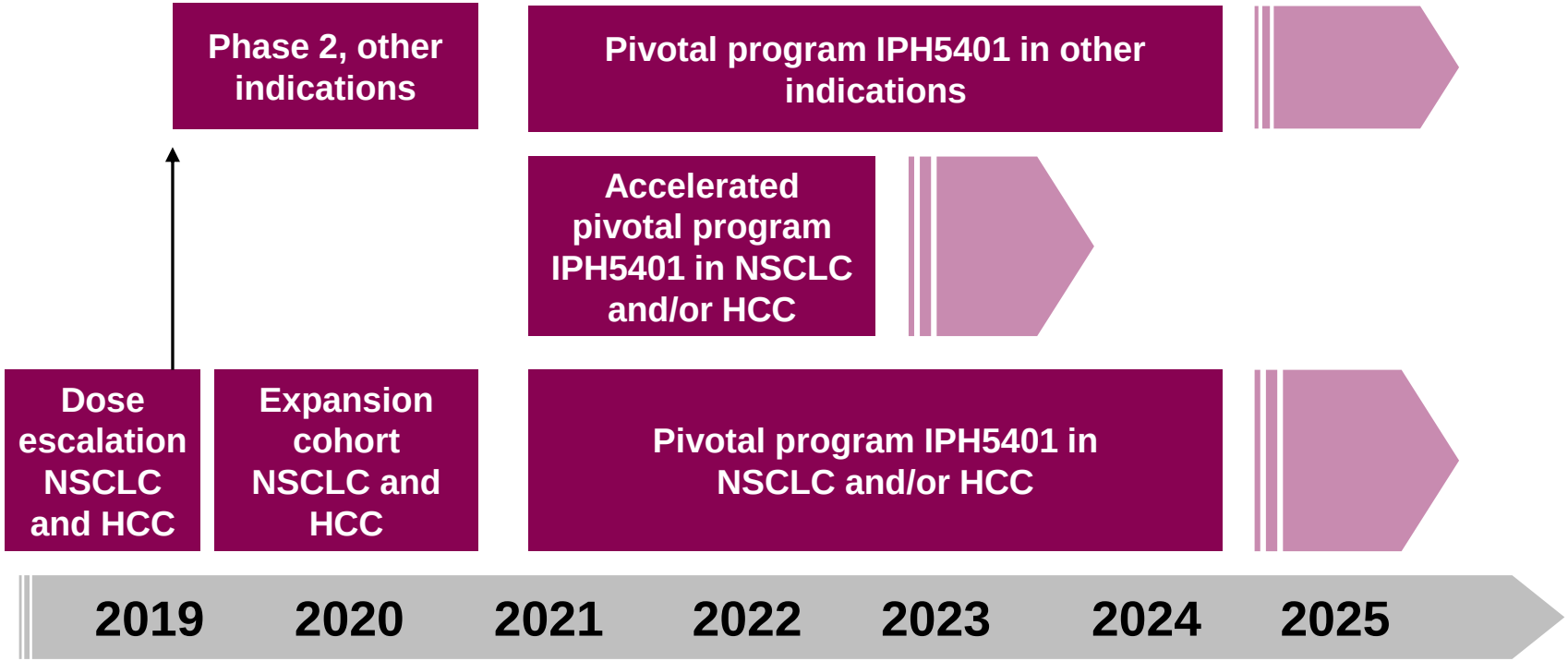


Cohort expansion part:
primary endpoint: ORR
(Simon 2-stage) design

NSCLC (secondary resistance to PD1/PDL1 blockers)	Stage 2
HCC (PD1 naïve)	Stage 2

~ 40 patients per indication

PHASE 1 TO START 2H2018



All elements of study design and dates subject to validation.

Potential Biologics License Application

ABUNDANT LIFE CYCLE OPPORTUNITIES

A COHERENT VISION OF MULTIPLE INDICATIONS, LINES OF THERAPIES AND DEGREE OF RESISTANCE

Tumor type	Setting
NSCLC	Secondary resistance to PD1/PDL1 blockers, in combination with durvalumab
HCC	PD1 naïve, in combination with durvalumab
UCC	IO untreated patients in combination with PD1/PDL1 agent

MedImmune
AstraZeneca

Tumor type	Setting
NSCLC	IO untreated patients
HCC	1st line setting
UCC	Earlier settings

Tumor type	Setting
Other tumor types (such as RCC, CRC, breast cancer,….)	Under discussion

SUMMARY

1 Inhibition of C5aR signaling increases effector cell infiltration and function in the TME
Long-term failure rates of PD-1/L1 therapy create demand for combination strategies

2 Prioritization of indications based on C5aR expression and medical need
Clinical collaborations enhance program value
Smart study design accelerates Proof-of-concept
Limited dose-escalating part based on good tolerability

3 Substantial market potential across selected tumor indications

NEXT GENERATION IO

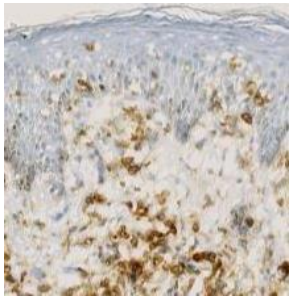
3 STRATEGIC KEY PILLARS

1	2	3
NK cells checkpoints (NKCP)	**Tumor targeting (TAg)** **IPH4102** (target: KIR3DL2)	**Tumor Microenvironment (TME)**

KIR3DL2 IS WIDELY EXPRESSED ON T CELL LYMPHOMAS

- KIR3DL2 is specifically expressed on cutaneous and circulating cutaneous T-cell lymphomas (CTCL) cells (various grades and subtypes):
  - > Expressed by ~65% of all CTCL patients
  - > Expressed by up to 85% of CTCL cells in certain aggressive subtypes, in particular Sézary Syndrome (SS) and transformed mycosis fungoides (tMF)
  - > Expressed by a subset of NK and T-cells
  - > Not expressed on other normal tissue
- Also expressed in PTCL (~50%) and ATLL (~80%)

SS pt, grade IIIB
87% KIR3DL2^{+} tumor cells[1]



CTCL: cutaneous T cell lymphoma; PTCL: peripheral T cell lymphoma; ATLL: adult T cell leukemia/lymphoma

Battistella et al., 3WCCL poster 2016 1. Internal data

IPH4102: MODE OF ACTION

PROMISING ACTIVITY IN SÉZARY SYNDROME

- IPH4102 : first-in-class anti-KIR3DL2 humanized cytotoxicity-inducing antibody
- Designed to selectively destroy KIR3DL2-expressing CTCL cancer cells:
  - > upon binding to the receptor, the Fc domain of IPH4102 activates antibody dependent cell-mediated cytotoxicity (ADCC)
  - > antibody-dependent cell-mediated phagocytosis (ADCP) is also activated

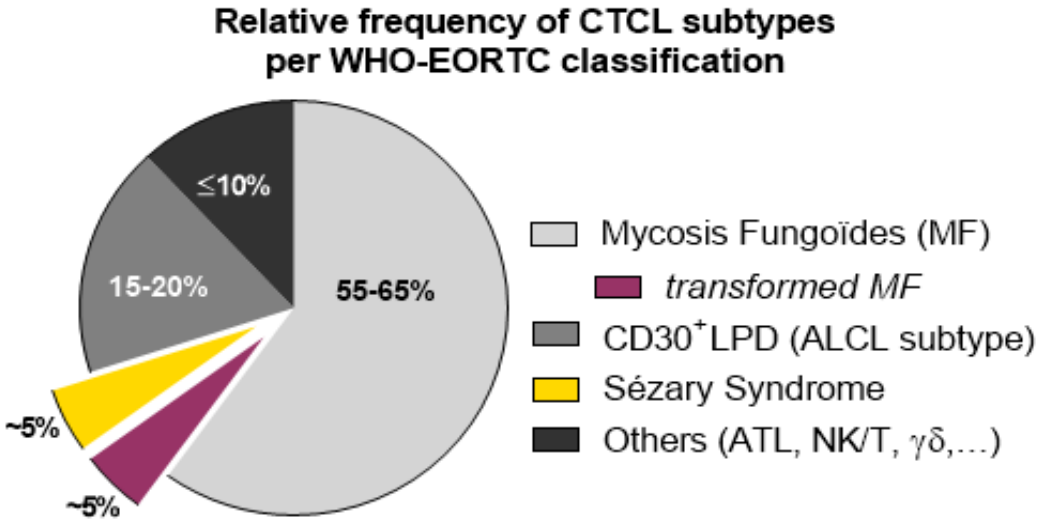
- Good safety profile and promising activity demonstrated from a dose-escalating part of an ongoing Phase 1 study investigating IPH4102 in patients with Sézary Syndrome, an advanced form of CTCL

WHAT IS CTCL?

- Non Hodgkin's lymphoma, originating from T cells and with a tropism for the skin
- 4% of Non Hodgkin's Lymphoma
  - > ~ 1 / 100,000 (6,000 new cases for the US + EU)
  - > Rising annual incidence in US - ↑ by 2.9 per million per decade
- Clinically:
  - > Median age at diagnosis of 55-65 years
  - > Pronounced cutaneous involvement with debilitating pruritus
  - > Lymph nodes, viscera, and blood (Sézary Syndrome) may be involved
  - > Elevated risk of infections

Agar et al, JCO 2010; Kempf et al, Blood 2011; Willemze, Blood 1997; Willemze et al, Annals Oncol 2011; Kim et al, Arch Dermatol 2003; SEER, 2017

EPIDEMIOLOGY OF CTCL (1)



Nr new cases/yr	5-yr overall survival
6,000	
3,300-3,900	20-95%
150-300	≤ 15%
500-1000	76-96%
150-300	~ 10%
600	≤ 20%

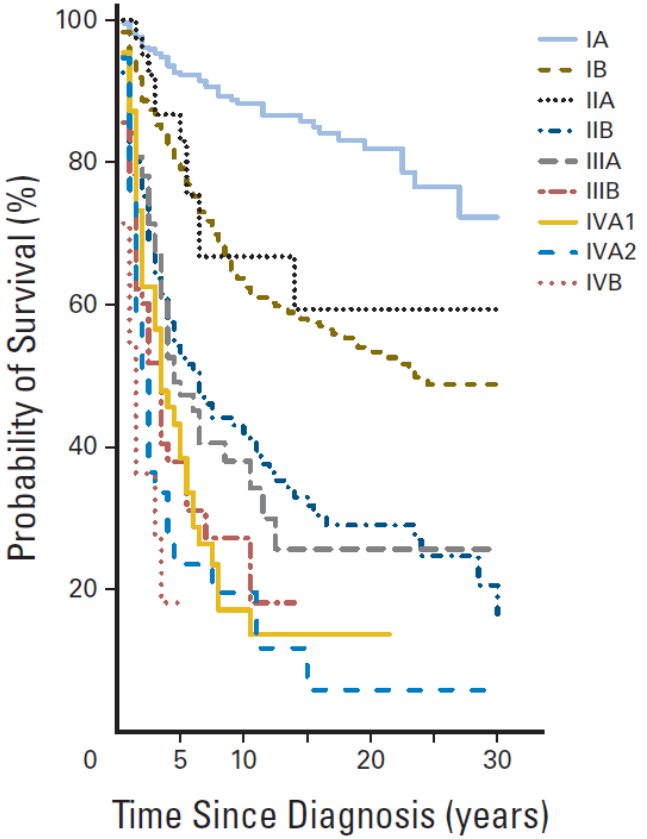
LPD: lymphoproliferative disorder. ALCL: anaplastic large cell lymphoma
ATL: Adult T cell lymphoma

Agar et al, JCO 2010; Kempf et al, Blood 2011; Willemze, Blood 1997; Willemze et al, Annals Oncol 2011; Kim et al, Arch Dermatol 2003

EPIDEMIOLOGY OF CTCL (2)

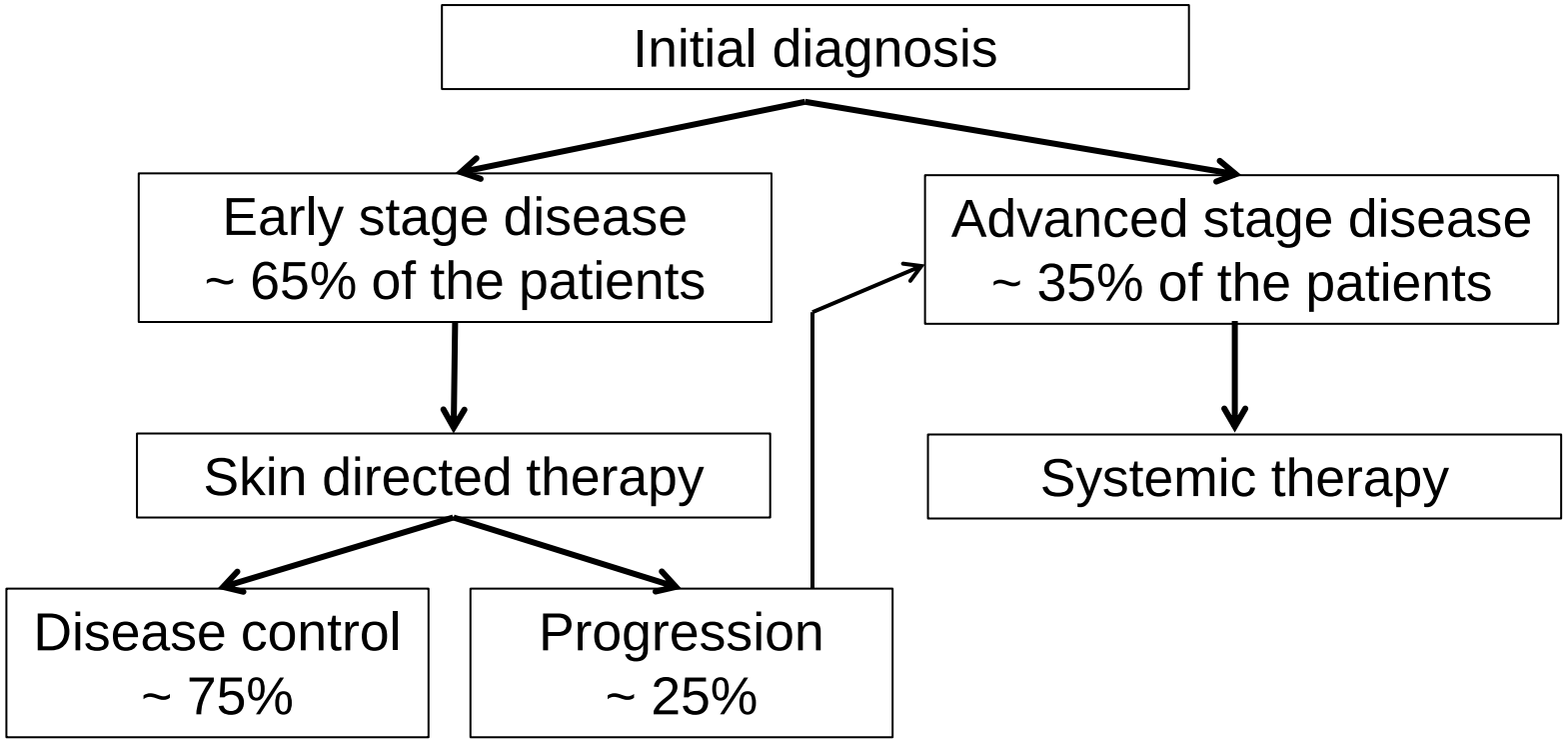
- Besides the histological subtypes, prognosis and survival of CTCL are strongly linked to **clinical stage**

- **Other poor prognostic factors**: age >60 years, large cell transformation (LCT) in skin, increased Lactate Dehydrogenase (LDH) and extracutaneous involvement



Agar et al, JCO 2010. Scarisbrick et al., 2015

TREATMENT OF CTCL
OVERVIEW



STANDARDS OF CARE IN CTCL

LIMITED TO MYCOSIS FUNGOIDES (AFTER FAILURE OF LOCAL THERAPIES)[1]

	Preferred therapies
1st line	Bexarotene, bexarotene-based combinations
2nd line	Interferon, methotrexate, gemcitabine, liposomal-doxorubicin
3rd line	Methotrexate, CHOP, palatrexate
4th line	Romidepsin

Lines are softly defined in CTCL and physicians frequently interchange drugs sequence

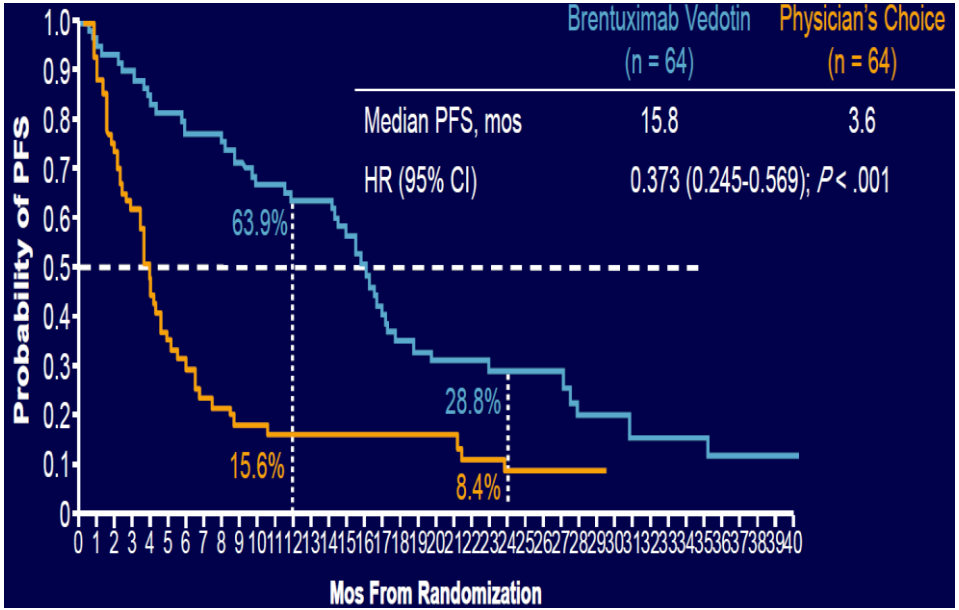
[1] May further vary between stage IB-IIB and > IIB

NCCN Guidelines, 2017. KOL interviews conducted by IPH, 2017

TREATMENT OF CTCL

NEW AGENTS WITH ACTIVITY: BRENTUXIMAB

- Brentuximab vedotin (Anti CD30 ADC):
  - > CTCL (CD30 positive; excl. SS): phase 3 study (ALCANZA) against investigator's choice (methotrexate/bexarotene) (128 pts)
  - > ORR4: 61 vs 8% (p < 0.001); med PFS: 15.8 vs 3.6 months (HR=0.37, p < 0.001)
  - > Polyneuropathy: 67% vs 6%; 14% RX discontinuation
  - > Drug approved by FDA and EMA



Horwitz SM, et al. ASH 2017

MOGAMULIZUMAB, A CCR4 INHIBITOR, IN CTCL

NEW AGENTS WITH ACTIVITY: MOGAMULIZUMAB

372 pts with MF or SS, in failure post ≥ 1 systemic therapy, randomized between mogamulizumab and vorinostat

Group [1]	PFS (mos) [1,2]	ORR	Toxicity
Mogamulizumab	7.7	28%	↑ Infusion related reaction, cutaneous toxicity
Vorinostat	3.1	5%	↑ nausea, diarrhea, fatigue, thrombocytopenia, decreased appetite, dysgueusia, renal
HR, p value	0.53 p< 0.0001		

[1] mos: months; HR: hazard ratio; ORR objective response rate

[2] Primary endpoint: PFS, using global composite response score based on skin, blood, lymph nodes, and viscera

Kim YH, et al. ASH 2017. Abstract 817.

STANDARDS OF CARE IN CTCL

HOW WILL MYCOSIS FUNGOIDES BE TREATED IN THE FUTURE?

KOLs opinion:

Bexarotene likely to stay the primary agent in 1st line (oral)

Strong impact of brentuximab & mogamulizumab in later lines

	Predicted preferred therapies
1st line	Bexarotene, bexarotene-based combinations
2nd line	Older drugs, brentuximab, and mogamulizumab competing in 2nd/3rd line
3rd line	
4th line	**Still remaining a major unmet medical need**

KOL interviews conducted by IPH, 2017.

CTCL

FOUNDATIONS OF OUR CLINICAL DEVELOPMENT PLAN

- Single agent approach after 2 lines of prior systemic therapy, including biologics
- Multiple different subtypes with a variable prognosis
- Variable stages (IB-IV)
- Complex treatment algorithms
  - > Variable local therapies before reaching the stage of advanced CTCL
  - > May vary among institutions
- KIR3DL2 positivity
  - > About 60% overall
  - > And biologically viewed as essential for the efficacy of IPH4102

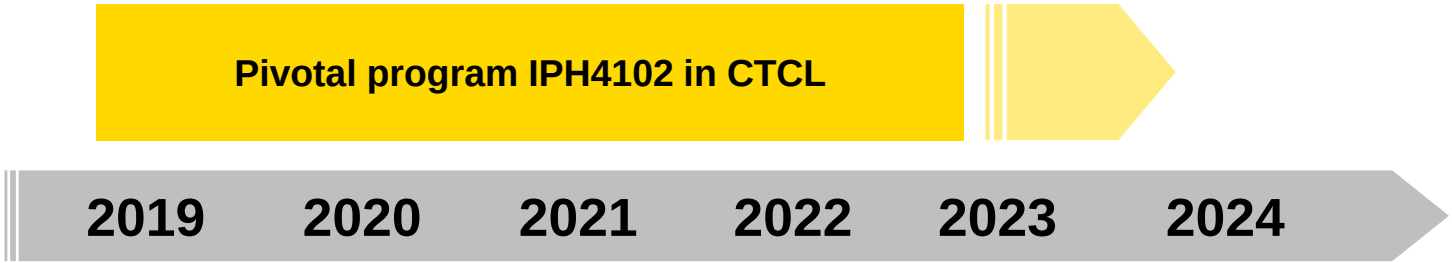
Supports a randomized program

Phase 2-3 design to explore biomarker strategy

CTCL

CLINICAL DEVELOPMENT PROGRAM[1]

- Population: advanced after 2 lines of prior systemic therapies, including brentuximab / mogamulizumab
  - > Leveraging IPH4102 in patients with unmet medical need
- Randomized program of single agent IPH4102
- Comparator: investigator choice (gemcitabine, vorinostat)
- Phase 2 component to gauge the level of antitumor activity and to assess the need for KIR3DL2 positivity



Potential Biologics License Application. 1. All elements of study design and dates subject to validation.

SÉZARY SYNDROME
CLINICAL FEATURES AND SIMPLIFIED TREATMENT APPROACH

- Leukemic variant of CTCL – stage IV in all cases – poor prognosis
- Systemic therapy is the standard of care
- Older drugs/approaches
  - > First line setting: extracorporeal phototherapy, bexarotene, interferon α (combinations > single agent)
  - > Alemtuzumab, HDAC inh, older chemo agents in 2nd line
  - > Stem cell transplantation but usage limited due to age
- Mogamulizumab
  - > Subset of patients in the MAVORIC trial suffered from SS
  - > Clear improvement of PFS (HR = 0.32, p< 0.0001) and ORR (37 vs 2%)

SS: Sézary syndrome; HR: hazard ratio; ORR: objective response rate

EA Olsen, J Am Acad Dermatol 2011;64:352-404. Kim YH, et al.
ASH 2017. Abstract 817. NCCN Guidelines, 2017

SÉZARY SYNDROME

OVERALL TREATMENT APPROACH IN 2018

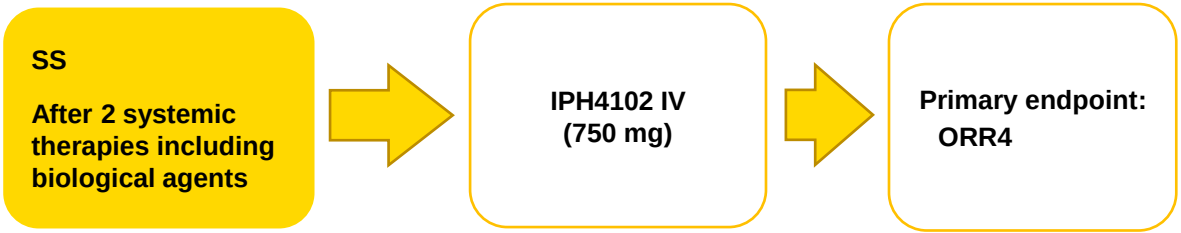
- ECP, bexarotene, Interferon α, Methotrexate, or combination of these approaches likely to stay the main approach in "1st line"
- Mogamulizumab likely to be approved (PDUFA date: June 4, 2018) and to penetrate the "2nd line" setting

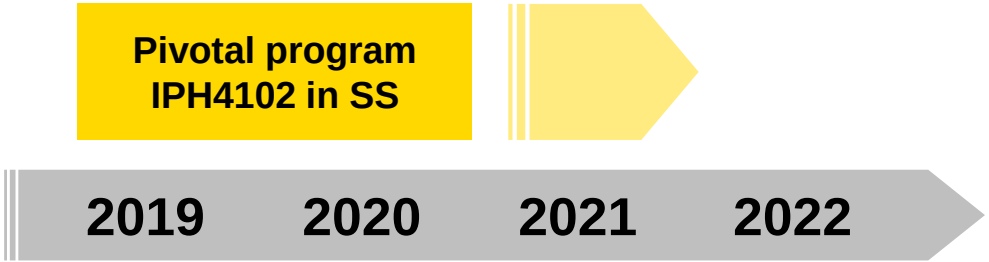
- 3rd + line setting continues to represent a major unmet medical need
  - > Activity of comparators, including approved ones (e.g. HDAC inh) is low
  - > Toxicity is an area of great concern
  - > Symptom control is badly needed

IPH4102 has demonstrated great promise in these 3 areas, paving the way for a pivotal program in 3rd line SS

PIVOTAL PROGRAM IN SÉZARY SYNDROME

STUDY DESIGN – POTENTIAL ACCELERATED APPROVAL





Regulatory consultations

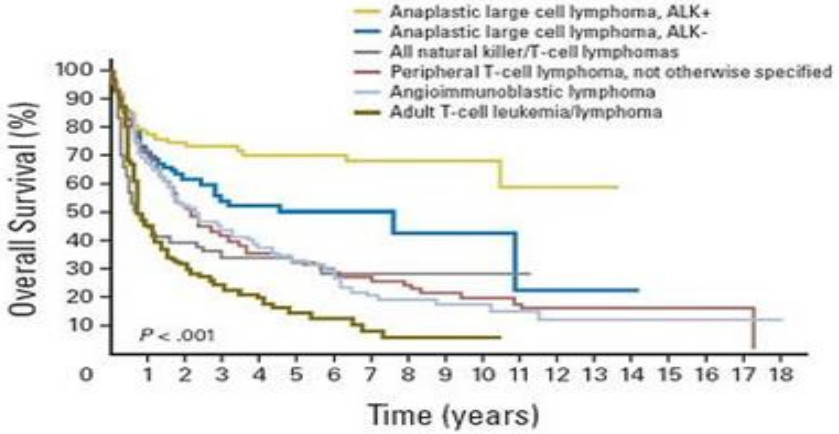
1. Preclinical data ✓
2. "Isolation" of SS ✓
3. ORR4 as 1ary endpoint, PFS as key 2ary endpoint ✓
4. Randomized design in small patient population using a calibration design ✓
5. Single arm approach under discussion, depending on cohort expansion data and mogamulizumab label ○

Potential Biologics License Application. All elements of study design and dates subject to validation.

POTENTIAL DEVELOPMENT PATHS IN OTHER LYMPHOMAS

PTCL

- PTCL represent ~10% of all NHL WW
- Several subtypes with variable response to therapy and outcome
- ~ 50% express KIR3DL2



Standard of care

	PTCL	Incl. ALCL
1st line	Chemo (CHOP-like) at times followed by transplantation if possible	
2nd line*, Salvage options	Gemcitabine, oxaliplatin, palatrexate§, combination chemo (DHAP, GEMOX) romidepsin§, belinostat§	
		Brentuximab vedotin

*In Japan, mogamulizumab is approved in r/r CCR4-positive PTCL. § approved in the US only

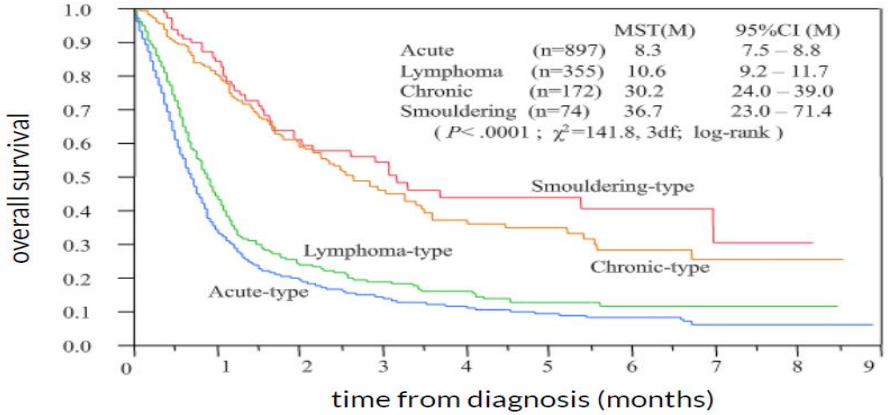
In total, in contrast to B cell lymphomas, PTCL remains a major medical challenge

International TCL Project JCO 2008

POTENTIAL DEVELOPMENT PATHS IN OTHER LYMPHOMAS

ATLL

- ATLL prevalence follows the distribution of the oncogenic HTLV-1 virus
  - > <10% of all PTCL WW (~25% in Japan)
  - > Annual incidence: WW: ~1,400; Japan: ~700-1,000
- Several subtypes with variable response to therapy and outcome
- KIR3DL2 expressed in ~ 80% of the patients



Standard of care

	Lymphoma	Acute
1st line*	Chemo (CHOP-like) – Clin. trial	IFN, zidovudine – Clin. trial
	Consolidation for allo SCT	
2nd + line*	No SOC	No SOC

*In Japan:
- Mogamulizumab is approved in 1st and 2nd lines.
- -80-100 ATLL patients are transplanted each year.

Shimoyama Classification – OS data, ESMO 2012

CLINICAL DEVELOPMENT PLANS IN PTCL AND ATLL[1]

- High interest of the medical community

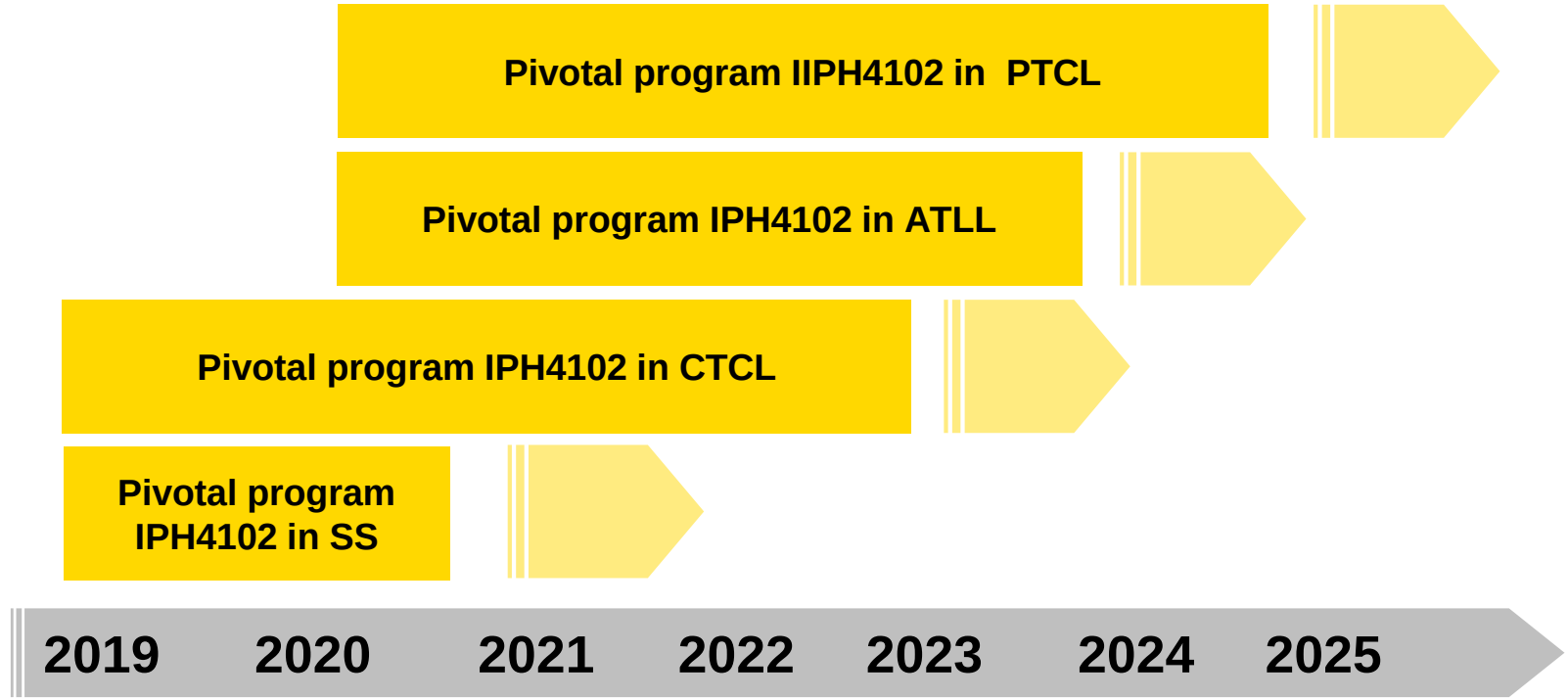
- PTCL
  - > Preliminary IHC data showing positive KIR3DL2 in about 50% of the pts
  - > Preliminary preclinical data supporting a combination approach with chemotherapy
  - > Phase 2-3 program testing combination + IPH4102

- ATLL
  - > High prevalence of KIR3DL2 expression (>80%) in the acute form (most frequent and poorest prognosis)
  - > Opportunity identified in 1st line, probably in combination with chemo; objective to raise the CR rate prior to SCT
  - > 2 staggered programs (EU/US vs Japan)

[1] All elements of study design and dates subject to validation

CLINICAL DEVELOPMENT PLAN[1] ACROSS PATIENT POPULATIONS

SUMMARY



Potential Biologics License Application. 1. All elements of study design and dates subject to validation.

TARGETING KIR3DL2 IN CTCL
PHASE 1 DOSE ESCALATION

Dr. Julia Scarisbrick

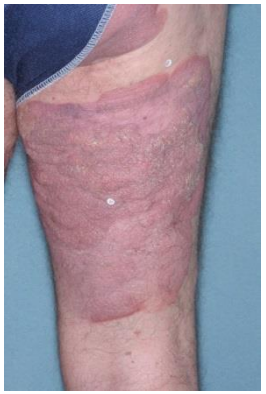
MBChB, FRCP, MD

University Hospitals Birmingham NHS Foundation Trust
St Thomas Hospitals
The London Skin Clinic

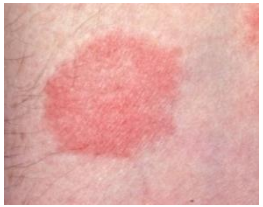
SIGNS AND SYMPTOMS OF MYCOSIS FUNGOIDES (MF) AND SÉZARY SYNDROME (SS)

- General
  - > Itching
  - > Disfigurement
  - > Pain
  - > Sleep disturbance
  - > Psycho-social disorders
  - > High disease burden
  - > Quality of life impairment

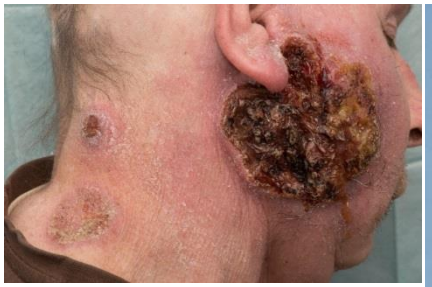
Early Stages



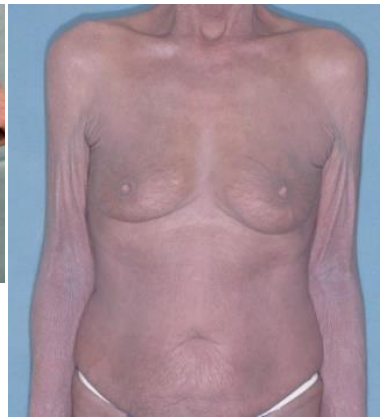
plaques



Advanced Stages



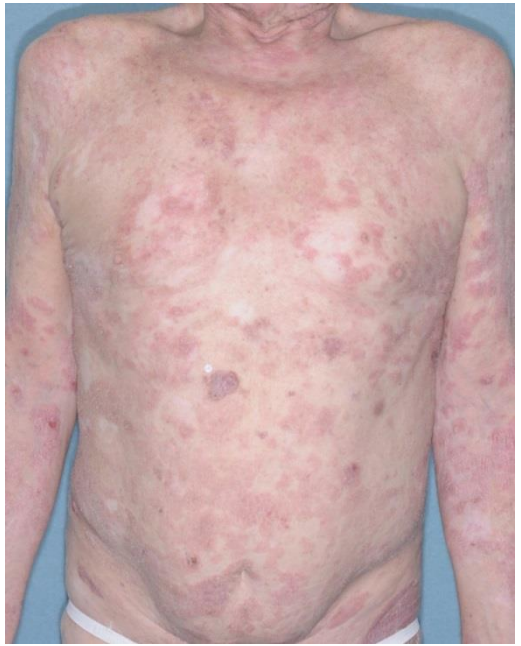
tumors



erythroderma

THERAPIES IN EARLY-STAGE CTCL (PATCH/PLAQUE)

- Skin directed therapy
  - > No treatment shown to be superior
  - > Typically associated with short response duration
  - > 50-60% of patients will have recurrent disease
  - > Few durable complete responses
  - > Life expectancy may be normal
  - > Morbidity may be significant
  - > Improve symptoms and quality of life



THERAPIES IN ADVANCED-STAGE CTCL

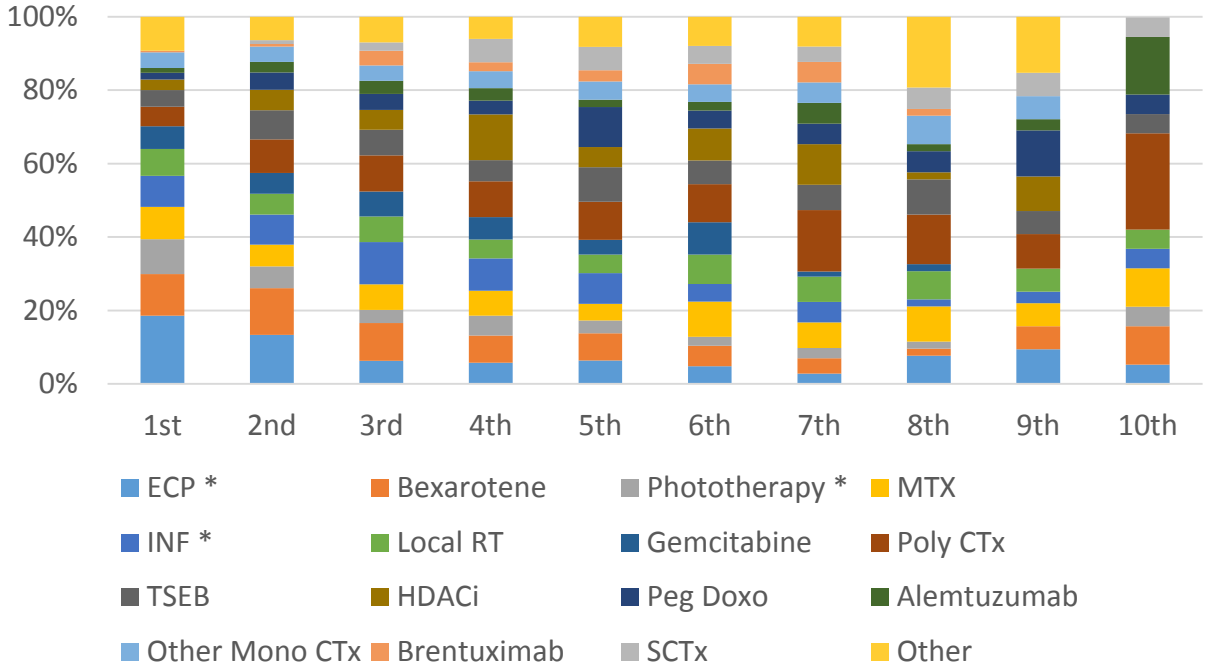
- Chemotherapy (1970's)
- Immunotherapy (interferon 1980's)
- Extracorporeal photopheresis (1987)
- Novel retinoids (bexarotene 1999)
- Monoclonal antibody therapy (1997/2001/2017)
- Autologous / Allogeneic stem cell transplants (2000)
- Histone deacetylase inhibitors (2013)
  (US: Vorinostat, Romidepsin)

- Treatment guidelines available from EORTC and NCCN[1]

[1] ***EORTC: Eur Org for Research and Treatment of Cancer. NCCN: National Comprehensive Cancer Network***

REAL-WORLD TREATMENT

Heterogeneity of treatment approaches were found, with up to 24 different modalities or combinations used as first-line and 31% of patients receiving 4 or more treatments



Modified from Quaglino et al, Ann Oncol. 2017

UNMET NEEDS IN CTCL

- Effective treatments
  - > Most have RR in 20-40%
  - > Most have short response duration 6-9 months
  - > Best combinations
- Effective symptom relief
  - > Patients have severe itch
  - > Sleep disturbance

SUMMARY TREATMENT GUIDELINES

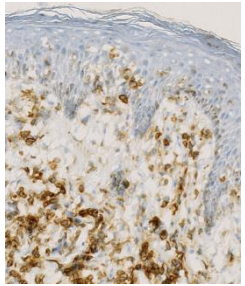
- Early-stage CTCL should be treated with skin directed therapies
- Advanced-stage CTCL require systemic therapy
  - > No algorithm for treatment which is typically patient specific
  - > No regime proven to improve survival
  - > Most patients receive multiple consecutive therapies
  - > Evidence-based treatment options needed

  - > Maintenance therapy to prolong progression free survival
  - > Patients should be entered into clinical trials

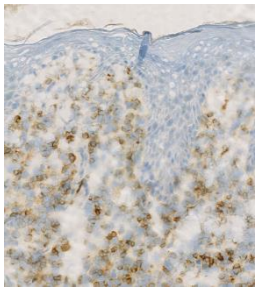
KIR3DL2 IS A THERAPEUTIC TARGET IN CTCL

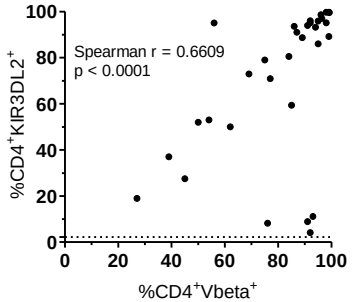
- KIR3DL2 belongs to the Killer Ig-like Receptor family that modulate NK and T cell activity
- KIR3DL2 is expressed on <10% normal T cells
- KIR3DL2 is widely expressed on CTCL cells (skin lesions and blood aberrant cells)
  - > Irrespective of disease clinical stage
  - > With a higher prevalence in Sézary syndrome (SS), CD30+ LPD and Mycosis fungoides with large-cell transformation
  - > KIR3DL2 may have prognostic significance in SS

Sézary syndrome



Transformed MF



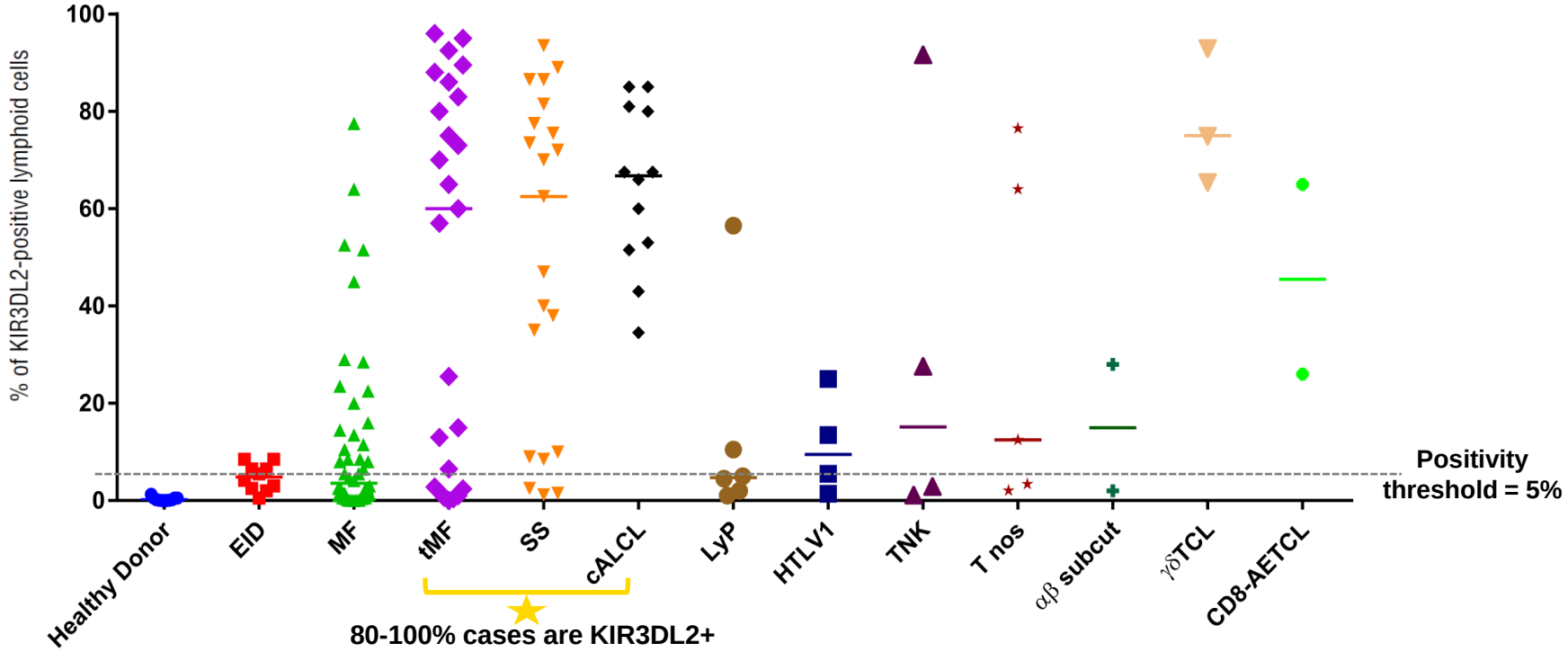


Correlation between KIR3DL2 and TCR-Vβ expression in Sézary syndrome (n = 32)

KIR3DL2 is considered a specific marker of CTCL, high therapeutic index

Marie-Cardine et al. Cancer Res 2014; Battistella et al. Br J Dermatol 2016; Hurabielle et al. Clin Cancer Res 2017

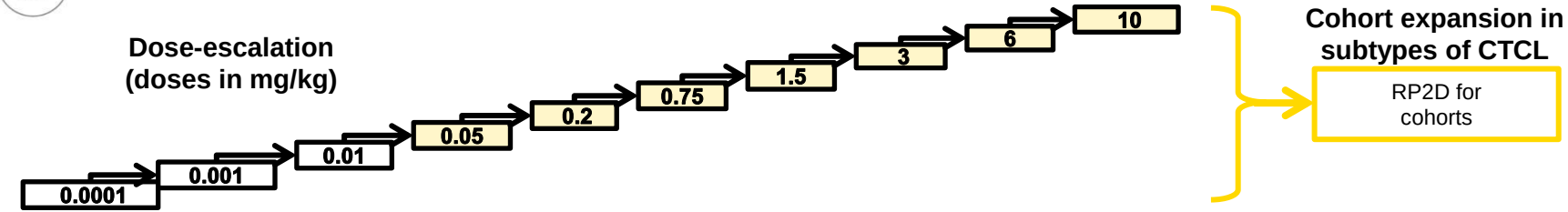
KIR3DL2 IS EXPRESSED ON MOST CTCL SUBTYPES



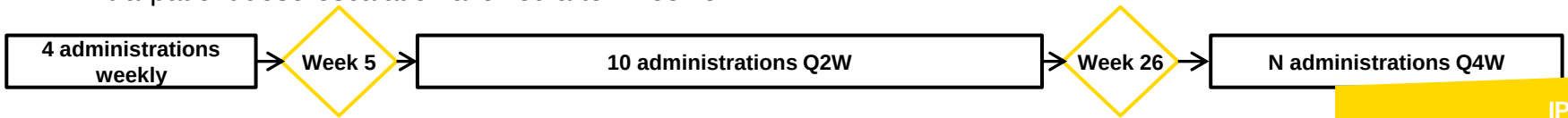
EID: erythrodermic inflammatory disease; MF: Mycosis Fungoides; SS: Sézary Syndrome; cALCL: primary cutaneous Anaplastic Large Cell Lymphoma; LyP: Lymphomatoid papulosis; HTLV1: (primary cutaneous) Human T-lymphotropic Virus positive T-cell lymphoma; TNK: extranodal NK-T cell Lymphoma; nos: not otherwise specified; subcut: subcutaneous panniculitis-like lymphoma; TCL: T-cell lymphoma; AETCL: aggressive epidermotropic T-cell lymphoma.

Battistella M. et al, Blood 2017

IPH4102-101 FIRST-IN-HUMAN PHASE 1 STUDY DESIGN AND OBJECTIVES



- Dose-escalation (10 dose levels – accelerated 3+3 design) followed by cohort expansion
- **Primary objective**: determination of Maximal Tolerated Dose (MTD) and Recommended Ph2 Dose (RP2D), overall safety
- **Secondary objectives**: clinical activity (criteria from Olsen et al 2011, JCO), PK/immunogenicity
- **Exploratory objectives**: changes in KIR3DL2+ cells in involved compartments
- **Key inclusion criteria**:
  - > Any CTCL subtype, ≥ 2 prior lines of systemic therapy, if MF/SS stage ≥ IB
  - > > 5% aberrant cells KIR3DL2pos in skin or blood
  - > Treatment until progression or unacceptable toxicity
- Intra-patient dose-escalation allowed after Week 5



BASELINE DISEASE CHARACTERISTICS (DOSE-ESCALATION)

	All doses N = 25
Age (years), **median** (min; max)	**71** (42; 90)
MF/SS CTCL type, n (%) Mycosis fungoides (MF) Sézary Syndrome (SS)	 4 (16) 20 (80)
Non MF/SS CTCL type, n (%) $CD4^+$ T-cell lymphoma, NOS	 1 (4)
Clinical stage at study entry (MF/SS), n (%) IB IIB IVA1	 1 (4) 3 (12) 20 (80)
No. of regimen (systemic) received, **median** (min; max)	**4** (2; 10)

SUMMARY OF ADVERSE EVENTS (AE) (DOSE-ESCALATION)

N = 25	Total	Grade 3	Grade 4
DLT	**0**	-	-
AE	**23 (92%)**	6 (24%)	2 (8%)
Related AE	**13 (52%)**	2 (8%)	**-**
SAE	**8 (32%)**	2 (8%)	2 (8%)
Related SAE	**2 (8%) ††**	**-**	**-**
AE causing treatment discontinuation	**1 (4%)**	**1 (4%)***	**-**
Fatal AE	**2 (8%)****		

n is the number of subjects having the given event, or an event in the given category at least once
DLT: Dose limiting Toxicity; (S)AE: (Serious) Adverse Event

†† Two patients had possibly related SAE: (i) one had grade 2 atrial flutter diagnosed by ECG without clinical symptoms. The patient was known for cardiac arrhythmia. The patient received 15 more administrations without reoccurrence of atrial flutter, (ii) one other patient had hepatitis occurring 6 weeks after last administration and treatment discontinuation due to PD. Considered unlikely to be related to IPH4102 by expert hepatologist.

* One patient discontinued treatment due to general malaise in context of disease progression.

** Two patients had fatal AE: (i) one unrelated death to S. aureus sepsis, (ii) one death caused by possibly related SAE of hepatitis (see ††).

ADVERSE EVENTS RELATED TO DRUG (DOSE-ESCALATION)
(REPORTED BY ≥2 PATIENTS, DATA CUTOFF 5/SEPT/2017)

	Related AE (N = 25)		
	All grades* n (%)	Grade 3 n (%)	Grade 4 n (%)
Any related AE	13 (52)	3 (8)	0
Lymphopenia	4 (16)	2 (8)	0
Asthenia	3 (12)	0	0
Nausea	2 (8)	0	0
Chills	2 (8)	0	0
Pyrexia	2 (8)	0	0
Arthralgia	2 (8)	0	0
Muscle spasm	2 (8)	0	0

n is the number of subjects having the given event, or an event in the given category at least once

EFFICACY OUTCOME (DOSE-ESCALATION)

DATA CUT-OFF 5/SEPT/2017

	Best Response in all patients Global N=25	Best Response in Sézary Syndrome patients		
		Global n=20	Skin n=20	Blood n=20
Best Response (n)				
CR	**1**	**1**	2	5
PR	**10**	**9**	10	8
SD	**12**	**8**	8	6
PD	**2**	**2**	0	1
ORR	**44 %**	**50 %**	60 %	65 %
ORR4, n (%)	**9 (36%)**	**8 (40%)**		
DOR (days) - median (min – max)	**251 (8.2 months)** (64 – 519+)	**302 (9.9 months)** (64 – 519+)		
PFS (days) - median (min – max)	**299 (9.8 months)** (28 – 610+)	**329 (10.8 months)** (28 – 610+)		

ORR: Overall Response Rate
ORR4: Rate of responses lasting ≥4 mo
PFS: Progression-Free Survival
DOR: Duration of Response

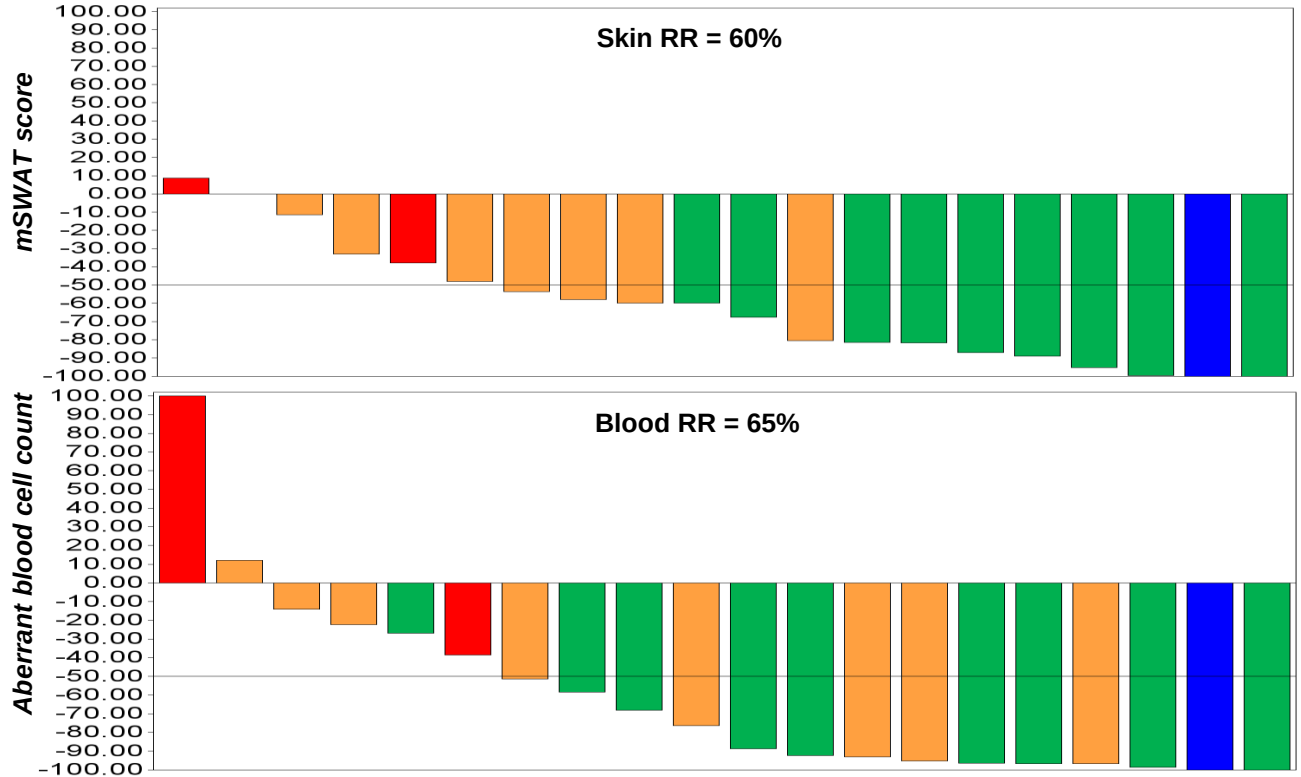
> Results for 25 patients (20 SS) treated with doses ranging from 0.0001 to 10 mg/kg
> All clinical responses are confirmed; 4 responses ongoing (DOR range 104 – 519 days)
> Median study follow-up time, 458 days (15 months)

MSWAT (MODIFIED SEVERITY WEIGHTED ASSESSMENT TOOL) IS USED TO MEASURE SKIN TUMOR BURDEN IN MF/SS

- Two assessments
    1. Lesion assessment – patch, plaque or tumor
    2. Body surface area involved
- Calculate body surface area affected by patch, plaque and tumor
- This is then multiplied by 1, 2, or 4 for patch, plaque and tumor respectively
- The sum of these 3 values is added and an overall SWAT value between 0-400 is achieved

%BSA patch + 2(% BSA plaque) + 4(% BSA tumor) = mSWAT/400

MAXIMUM PERCENT CHANGE IN MSWAT SCORE AND ABERRANT BLOOD CELL COUNTS IN SÉZARY SYNDROME PATIENTS



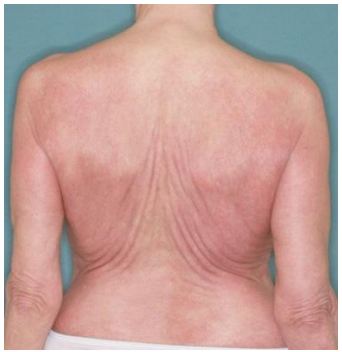
Best Global Response:

- CR
- PR
- SD
- PD

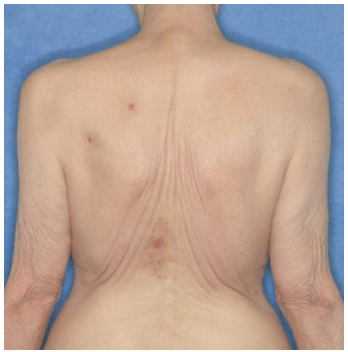
IPH4102

REPRESENTATIVE PICTURES OF RESPONDERS

- **Patient 11-005:**
  - > 77-year old female
  - > Sézary Syndrome (SS) diagnosed in NOV 2008
  - > 6 lines of previous therapies (incl. ECP + BEX + INFα, MTX, mogamulizumab, ECP + INFα + MTX, romidepsin, BEX+ INFα)
  - > Started at 0.05 mg/kg on 25JAN16
  - > Global PR since W10 (0.05 mg/kg), sustained at W64



Screening

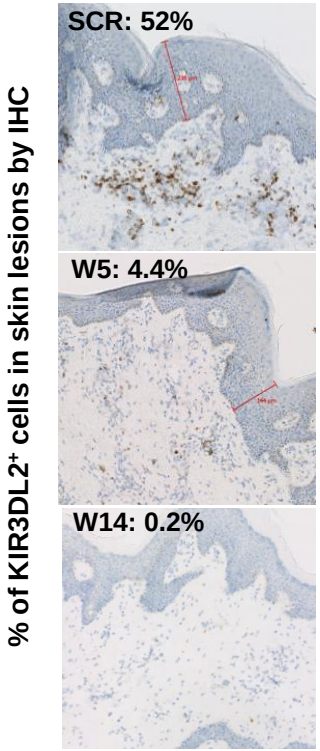


W64 sustained PR

EXPLORATORY/PHARMACODYNAMICS ENDPOINTS

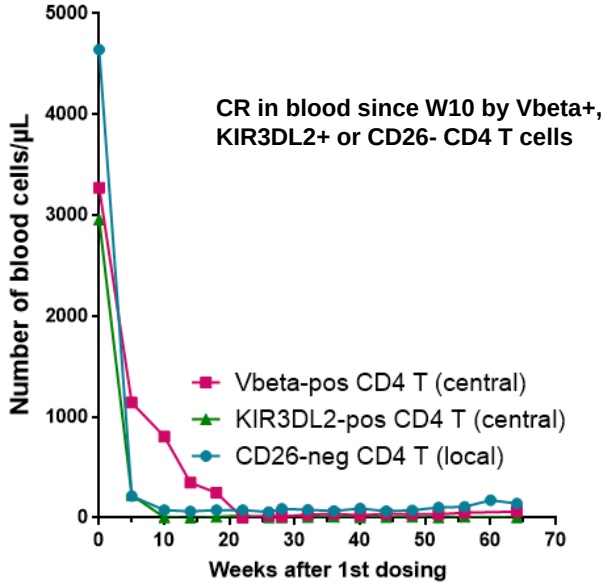
SKIN & BLOOD ASSESSMENTS / PT 11-005

SCR = screening



CD4/8 ratio in skin	mSWAT score
SCR: 49	SCR: 82.5
W5: 19	W5: 87
	W10: 36.5 PR
W14: 9	W14: 19.3 PR

- Treated skin lesions show decrease in CD4 and increase in CD8 lymphocytes
- Decrease in %KIR3DL2+ CD4 T-cells in skin/blood
- Sharp decrease in circulating Sézary cells in flow cytometry

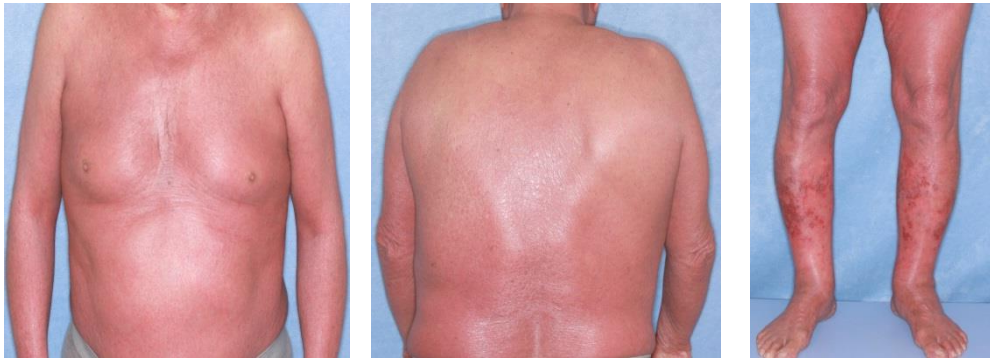


IPH4102

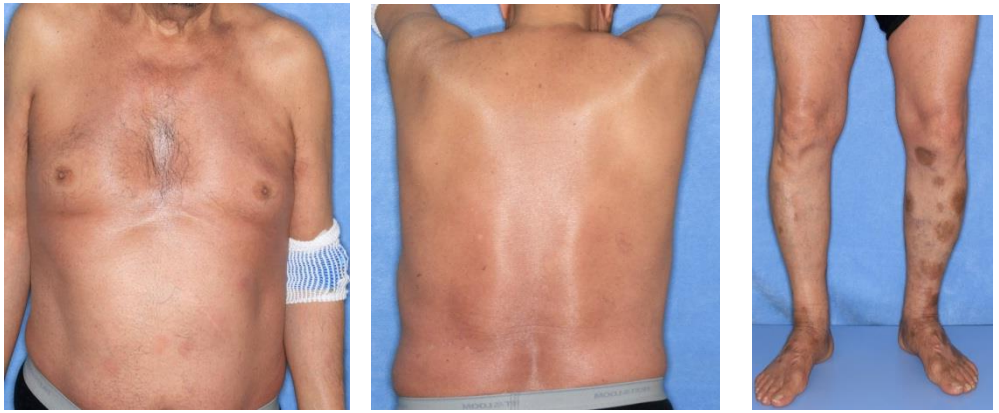
REPRESENTATIVE PICTURES OF RESPONDERS

- **Patient 11-024:**
  - > 75-year old male
  - > SS diagnosed in AUG 2011
  - > 6 lines of previous therapies (incl. MTX, INFα, vorinostat then mogamulizumab, BEX, pembrolizumab)
  - > Started at 3 mg/kg on 16OCT16
  - > Global PR since W14 (3 mg/kg), sustained PR at W28

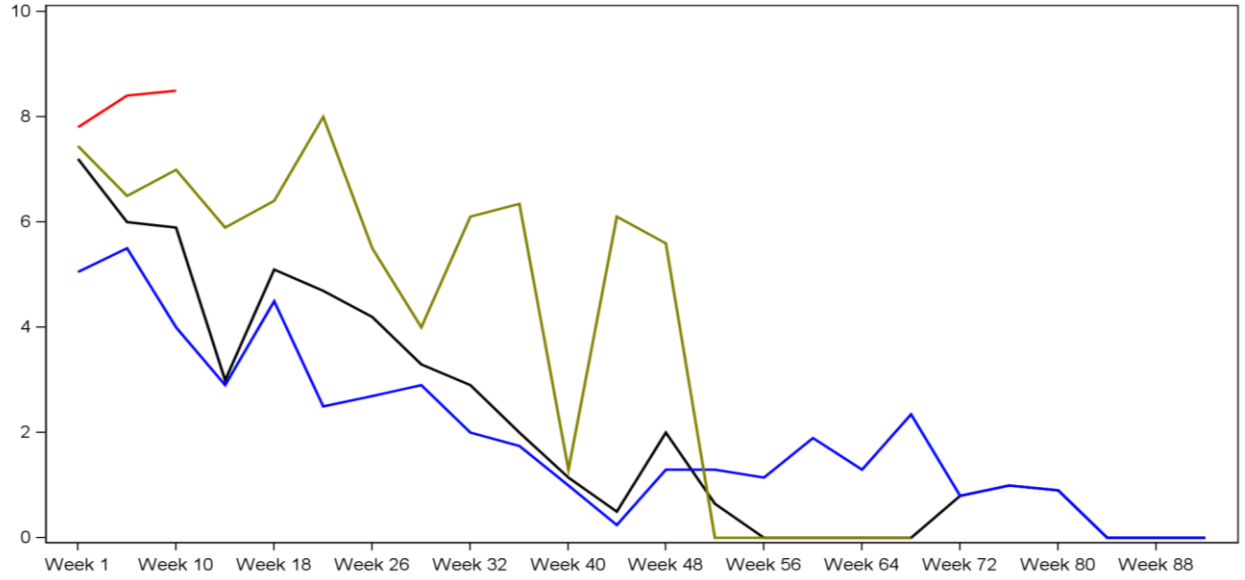
Screening



W28 Sustained PR



SIGNIFICANT PRURITUS IMPROVEMENT BY VAS SCORE



overall	20	18	18	16	17	15	15	15	15	10	6	5	6	4	3	3	3	3	2	2	2	1	1	1
CR/PR	10	10	9	9	9	8	9	9	9	6	3	2	3	3	2	2	2	2	2	2	2	1	1	1
obs SD	8	7	8	7	8	7	6	6	6	4	3	3	3	1	1	1	1	1						
obs PD	2	1	1																					

VAS: Visual Analogue Scale

IPH4102-101 SUMMARY (DOSE ESCALATION)

SAFETY, CLINICAL ACTIVITY AND BIOMARKERS

- IPH4102 Maximal Tolerated Dose was not reached: Recommended Ph 2 Dose is 10 mg/kg
- Well-tolerated in heavily pretreated (med. 4 prior lines) advanced CTCL patients
- Best global ORR is 44% in the overall population and 50% in SS
  - > In the Sézary population, median Duration of Response is 9.9 months and median PFS 10.8 months
- Pruritus is substantially improved in those with global response or stable disease
- Pharmacodynamic endpoints (monitoring of KIR3DL2-positive cells) are consistent with clinical activity results, confirming prompt elimination of neoplastic cells in skin and in blood

Expansion cohorts (SS, tMF) started accruing in July 2017 at the flat dose of 750 mg

ACKNOWLEDGEMENTS

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Nicolas Thonnart
Armand Bensussan

Histalim (Montpellier, France)
Laurence Maunier

Leiden University Medical Center (Leiden, Netherlands)
Maarten Vermeer

Guy's and St Thomas' Hospital (London, UK)
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Basem William

SKCC at Jefferson, Philadelphia (PA, USA)
Pierluigi Porcu

MDACC (TX, USA)
Madeleine Duvic
Auris Huen

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Carine Paturel
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Christine Paiva
Cécile Bonnafous
Arnaud Dujardin
Ariane Morel
Christian Belmant
Anne T. Martin
Hélène Sicard

NEXT GENERATION IO
3 STRATEGIC KEY PILLARS

1	2	3
NK cells checkpoints (NKCP) **monalizumab** (target: NKG2A)	**Tumor targeting (TAg)**	**Tumor Microenvironment (TME)**

MONALIZUMAB
COMBINATION STRATEGY OPPORTUNITY

Mohammed Dar
VP Oncology clinical development

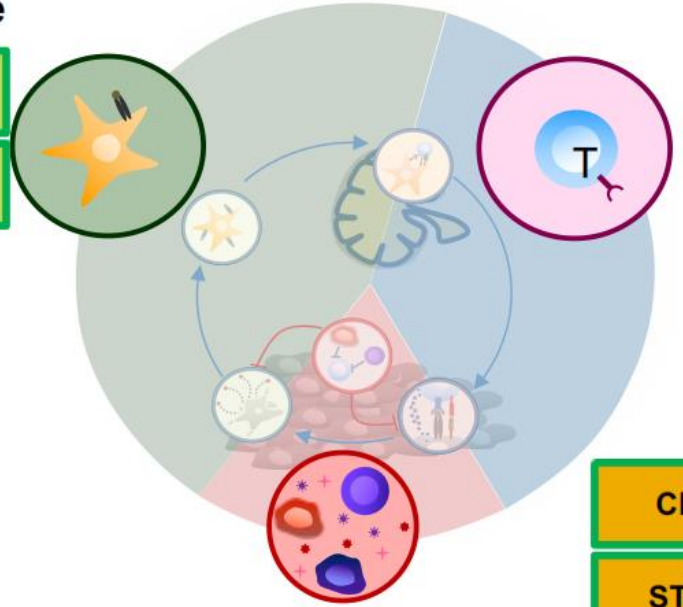
AstraZeneca MedImmune

NEXT-GENERATION IMMUNO-ONCOLOGY AT ASTRAZENECA/MEDIMMUNE

BROAD IO CLINICAL PROGRAM TO ENHANCE ANTI-TUMOR IMMUNITY

Prime new response

- TLR 7/8
- HDAC[1]
- DNA vaccine
- HPVE7[1]



Potentiate existing response

- PD-L1
- hOX40[2]
- PD-1
- CTLA-4
- GITR
- NKG2A

Reverse local immune-suppression

- CD73
- A2AR
- CXCR2
- STAT3
- IDO[1]
- IMCgp100[1]
- CSF-1R[1]
- TGFβR-1[1]
- CCR4[1]

Ongoing *Imfinzi* combination

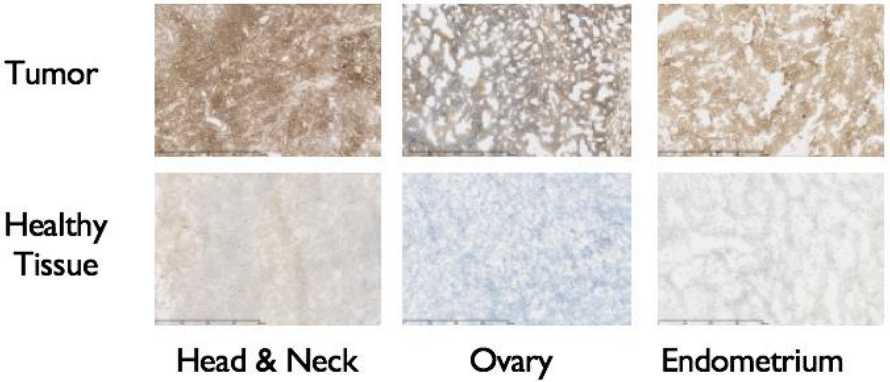
1. Clinical collaborations.
2. Combination with *Imfinzi* and tremelimumab.

Monalizumab

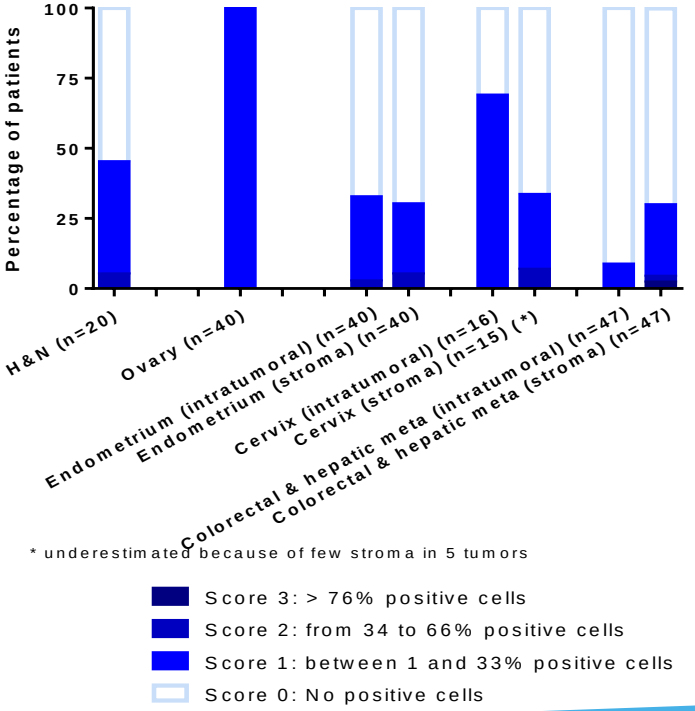
MONALIZUMAB (IGG_4 ANTI-NKG2A)

BLOCKS NKG2A/HLA-E MEDIATED SUPPRESSION OF NK CELLS AND CD8 T CELLS

HLA-E on tumor cells



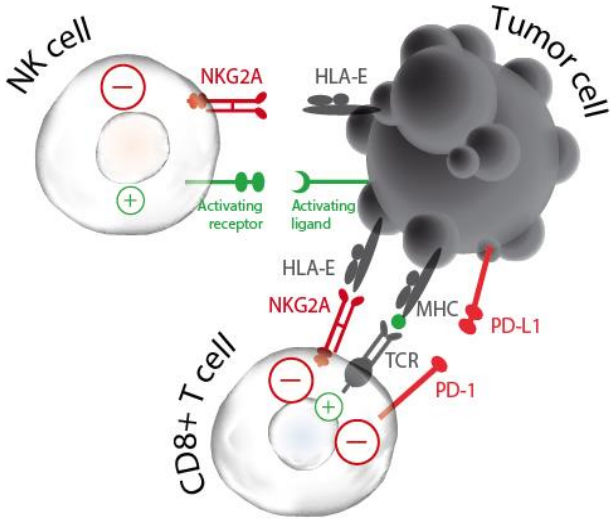
NKG2A on TILs

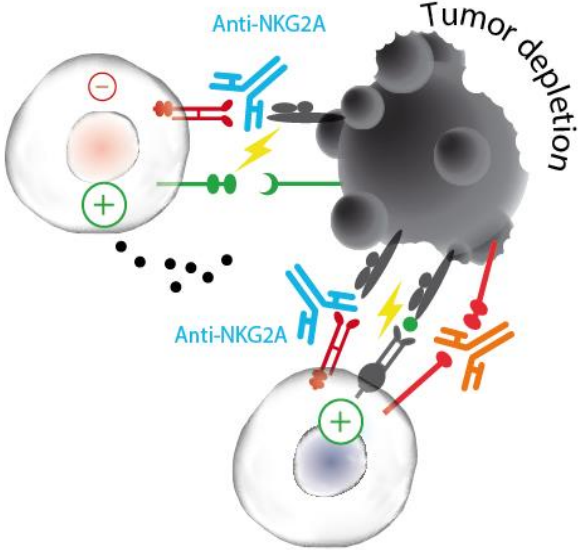


André et al. unpublished

RATIONALE FOR DURVALUMAB & MONALIZUMAB COMBINATION:

ENHANCE ANTI-TUMOR IMMUNITY BY NON-REDUNDANT, POTENTIALLY SYNERGISTIC PATHWAYS





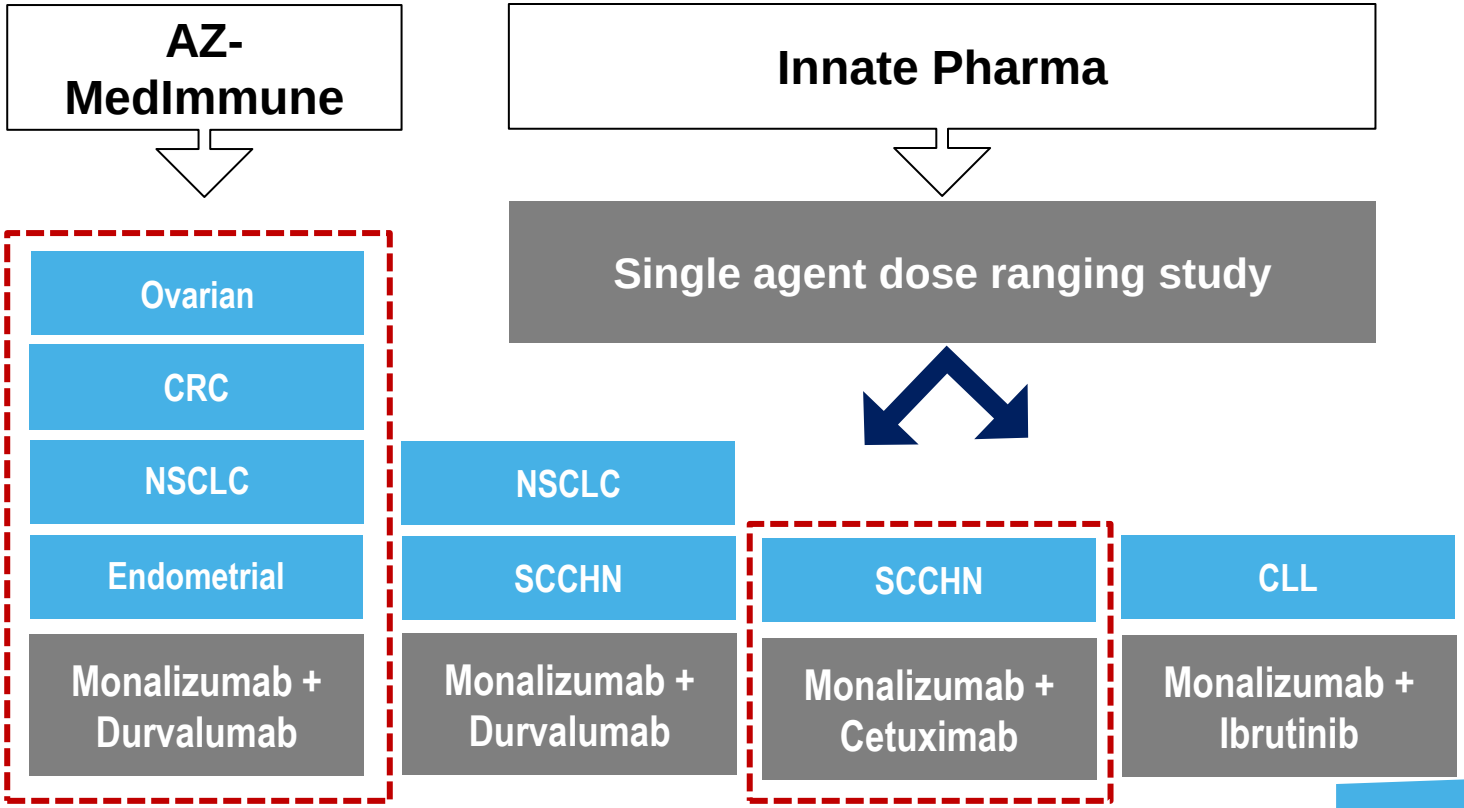
MONALIZUMAB – DEVELOPMENT STRATEGY

ADDRESS SIGNIFICANT MEDICAL NEEDS

1	Potentiate existing responses – IO sensitive tumors
2	Reverse resistance to CPI – IO sensitive tumors
3	Unlock activity of NK and T cells – IO resistant tumors

MONALIZUMAB – JOINT CLINICAL DEVELOPMENT PLAN

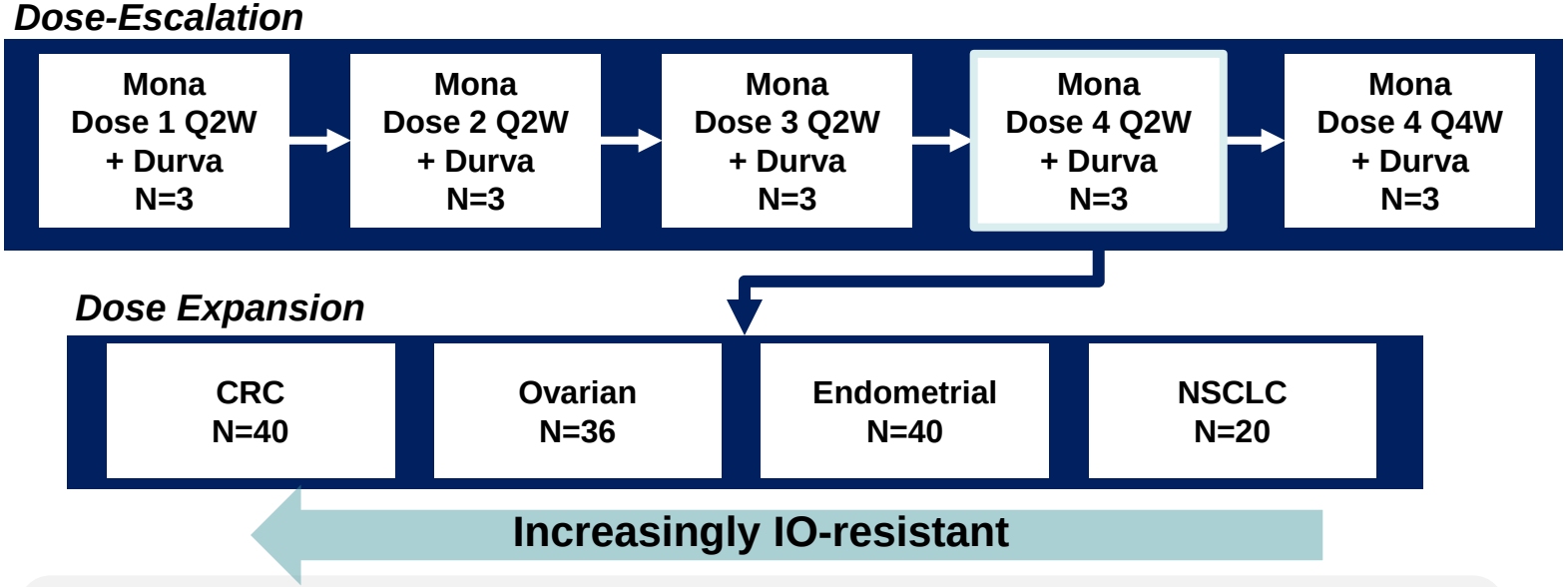
FOCUS ON COMBINATIONS



MONALIZUMAB – CLINICAL DEVELOPMENT PLAN

ONGOING PHASE 1 STUDY, DURVALUMAB + MONALIZUMAB

Data snapshot 09Feb2018. Database is open and data cleaning in progress; results subject to change



Safety Summary

- Planned dose-escalation completed without reaching MTD; no DLT reported
- Overall safety profile generally comparable to durvalumab monotherapy

MONALIZUMAB – CLINICAL DEVELOPMENT PLAN

MONALIZUMAB & CETUXIMAB COMBINATION

Rationale

- High level of HLA-E expression in SCCHN
- Cetuximab is approved in SCCHN, including in post-platinum setting
- Cetuximab-mediated ADCC is inhibited by HLA-E expression and this inhibition can be circumvented with anti-NKG2A treatment[1]
- Combination of monalizumab and cetuximab might provide greater antitumor activity than either drug alone

Evaluate safety and define MTD/RP2D of mona+cetux ✓

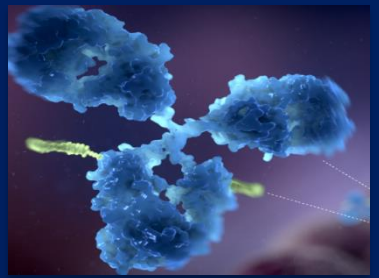
Assess antitumor activity of mona+cetux in 2L+ SCCHN — **Ongoing**

Explore additional combinations of mona+cetux — **Planned**

KEY DEVELOPMENT QUESTIONS FOR MONALIZUMAB

Understand which pts likely to benefit from Mona+Durva

Assess potential to combine with chemotherapy



Understand potential with tumor-targeting mAbs

Ongoing analysis of paired tumor and blood samples

Consider chemotherapy combination arms

Explore cetuximab-based combos

MARKET POTENTIAL AND PIPELINE NEWSFLOW

MONDHER MAHJOUBI

CHIEF EXECUTIVE OFFICER

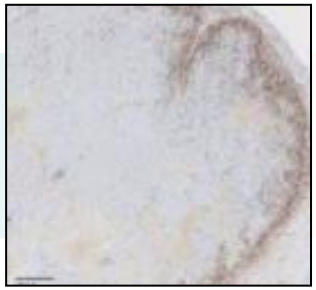
INNATE PHARMA – PIPELINE

BUILDING AN INNOVATIVE & DIFFERENTIATED PIPELINE

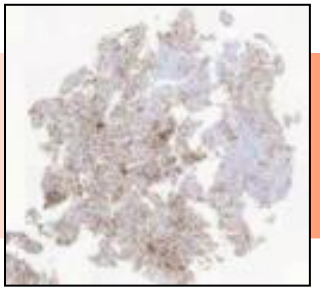
Noninflamed

No effective anti-tumor immunity

Anti-tumor immunity suppressed by TME



Sub-optimal or exhausted anti-tumor immunity



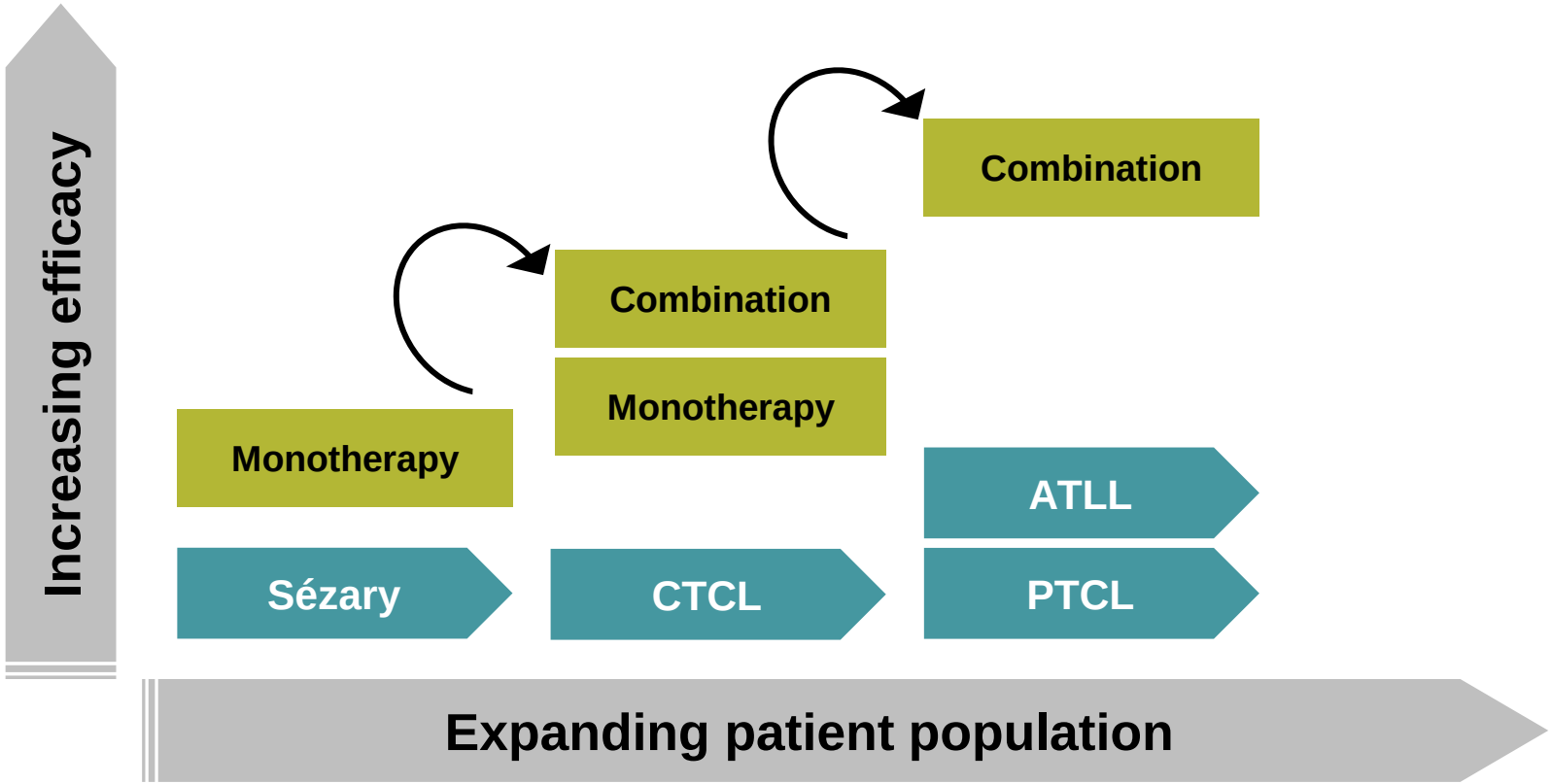
Inflamed

NK Bispecific Engagers	**IPH5401** Anti-C5aR	**Monalizumab** Anti-NKG2A
Antibody Drug Conjugates	**IPH53** Anti-CD73	**Lirilumab** Anti-KIR2DL1,2,3
	IPH52 Anti-CD39	**IPH4102** Anti-KIR3DL2
	IPH4301 Anti-MICA/B	

Adapted from Hedge et al., Clin Cancer Res, 2016

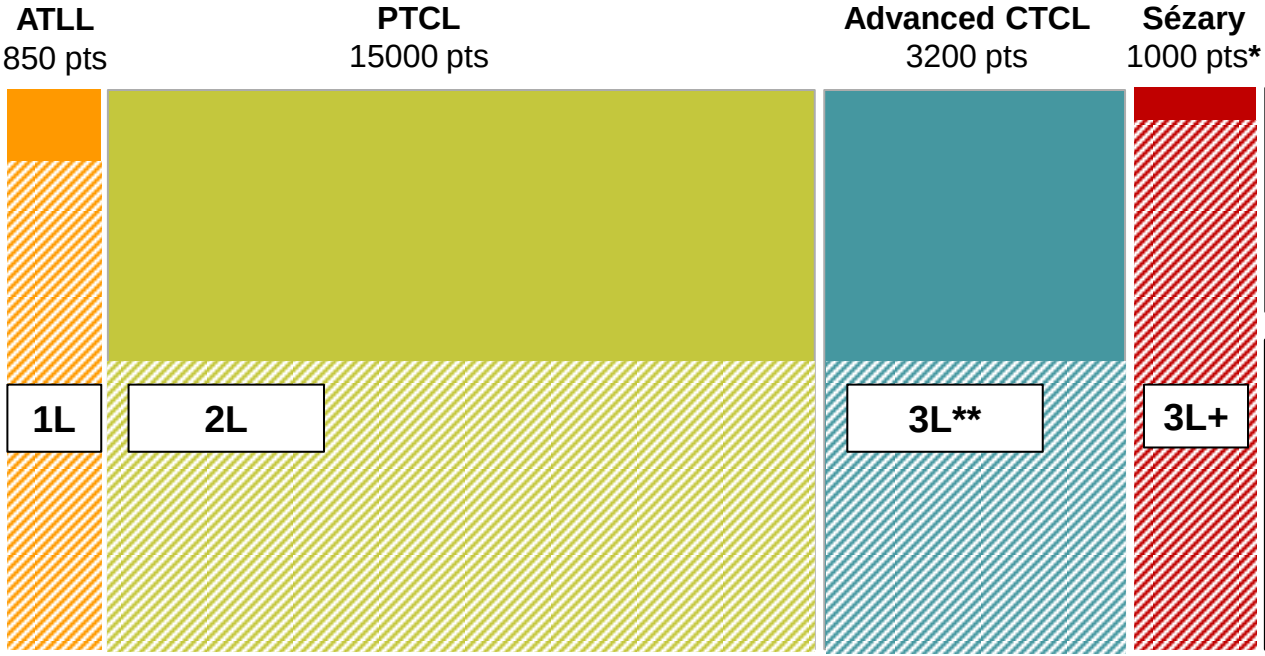
IPH4102 – TARGETING T-CELL LYMPHOMA

SÉZARY AS THE ENTRY POINT



IPH4102 – COMMERCIAL OPPORTUNITY

SIGNIFICANT POTENTIAL BEYOND SÉZARY



- 15% of all NHL
- Highly heterogeneous
- Medical need in late lines

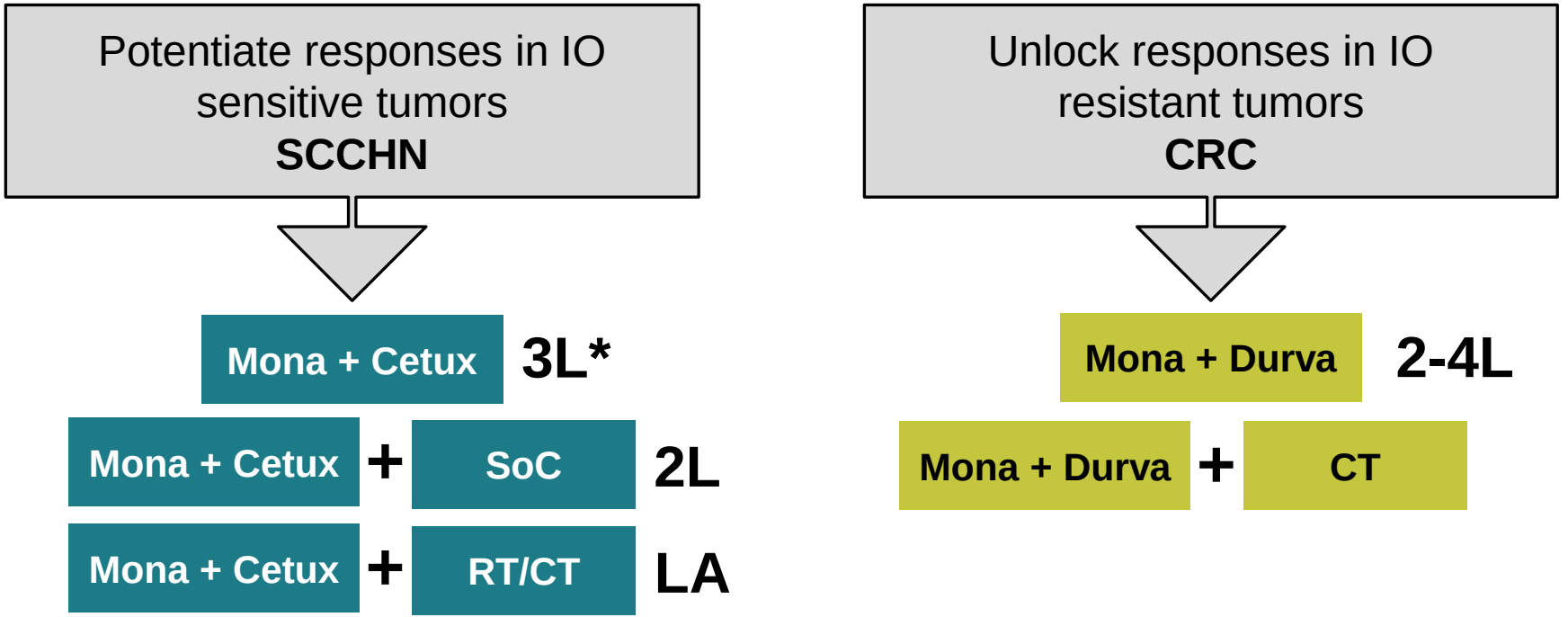
- Differentiated profile
- Biomarker driven therapy
- Premium pricing strategy
- LCM options

* Prevalence
** post mogamulizumab or brentuximab

Epidemiology data : Internal best current estimates of patient numbers based on external research

MONALIZUMAB – COMBINATION STRATEGY

LEVERAGE NON REDUNDANT & SYNERGISTIC PATHWAYS



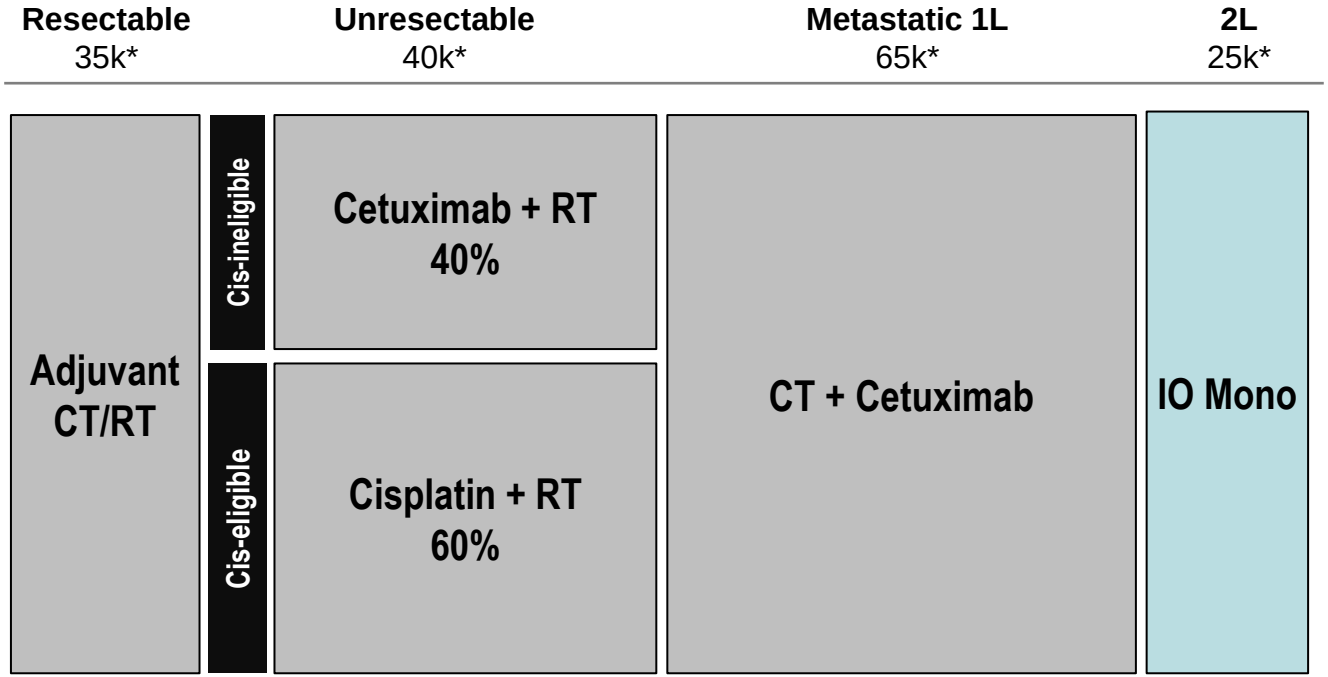
***3L: Potential fast to market opportunity**

L: line; RT: radiotherapy; CT: chemotherapy

MONALIZUMAB – COMMERCIAL OPPORTUNITY

SCCHN – CURRENT COMPETITIVE LANDSCAPE

IO SOC
Other SOC

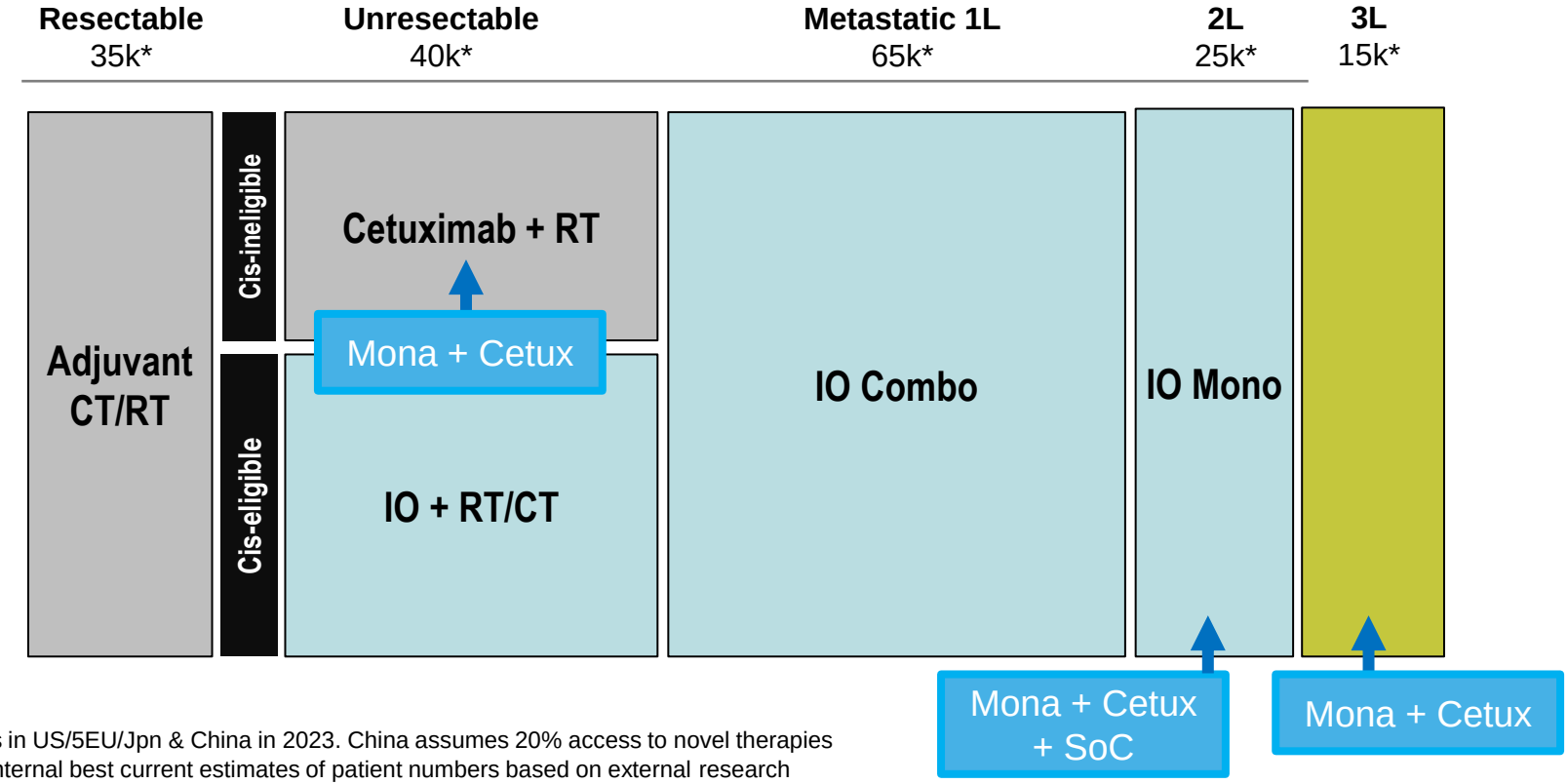


*Drug-treated patients in US/5EU/Jpn & China in 2023. China assumes 20% access to novel therapies
Epidemiology data : Internal best current estimates of patient numbers based on external research

MONALIZUMAB – COMMERCIAL OPPORTUNITY

SCCHN – FUTURE COMPETITIVE LANDSCAPE

IO SOC
Other SOC



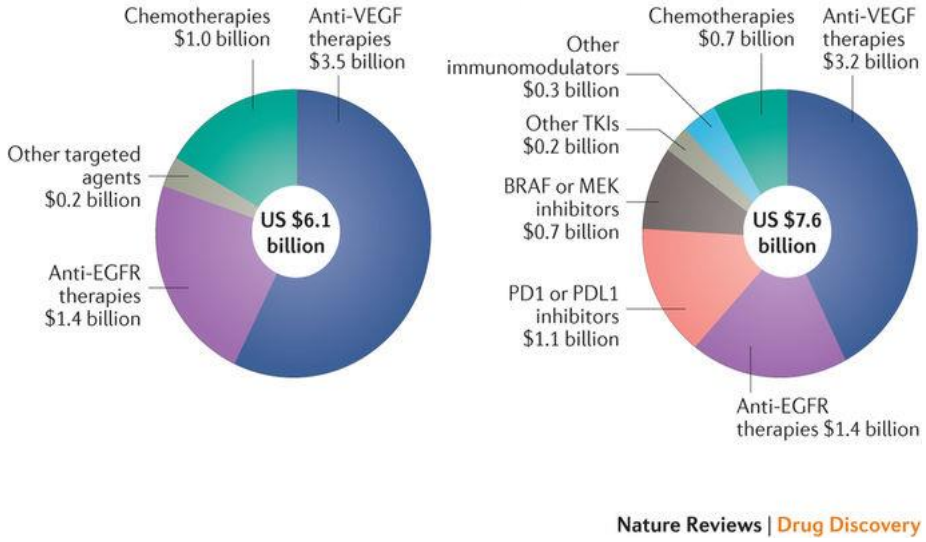
*Drug-treated patients in US/5EU/Jpn & China in 2023. China assumes 20% access to novel therapies
Epidemiology data : Internal best current estimates of patient numbers based on external research

MONALIZUMAB – COMMERCIAL OPPORTUNITY

CRC - THE NEXT BIGGEST OPPORTUNITY

- Third most common cancer worldwide
- ~1.1m deaths by 2030
- High unmet need in the metastatic setting
- Chemo + Bev or Cetux is SoC
- Limited options in late lines
- IO monotherapy approved in 3L MSI-high
- Large majority of patients are MSS and do not benefit from single agent IO
- Low efficacy bar in 3L

2016 **2026**



➔ **Increase EGFR / PD1-PDL1 IO share**

IPH5401– UNLOCK THE IMMUNE RESPONSE

IN COMBINATION WITH ANTI PD/PD-L1

Strategy

- Reverse IO resistance
- Enhance IO response
- Expand into IO refractory tumors

Tumor types	Incidence *	C5aR expression
NSCLC	290K	~80%
UCC	50K	~70%
HCC	110K	~70%
CRC	575K	60%
Gastric	258K	30-35%
TNBC	72K	13-27%
Prostate	621K	35%

* US/5EU & Japan

**drug treated 1st line patients, all stages, US & EU5

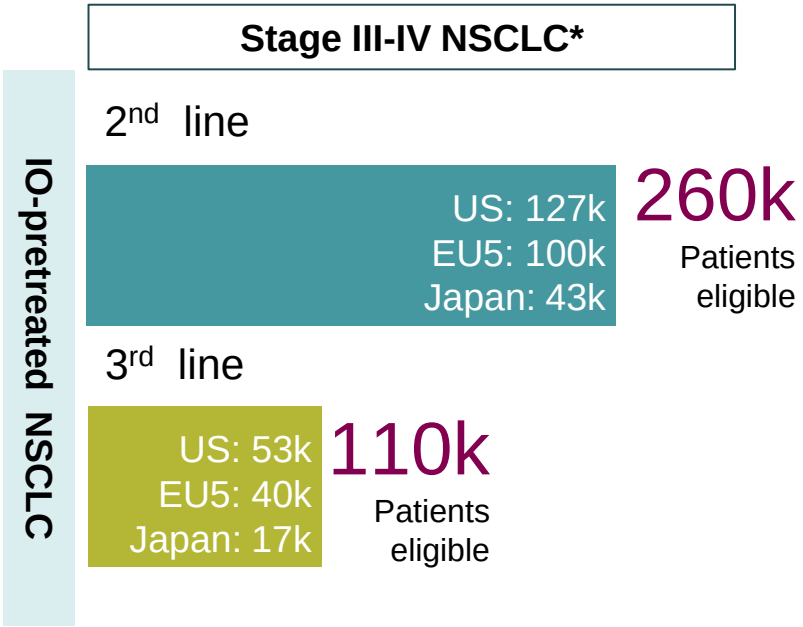
Epidemiology data : Internal best current estimates of patient numbers based on external research

IPH5401 – COMMERCIAL OPPORTUNITY

NSCLC – TREATING IO FAILURES

- **~1.6m** global lung cancer deaths
- IO transforming NSCLC management
- Vast majority of patients still fail IO

IO-pretreated patients

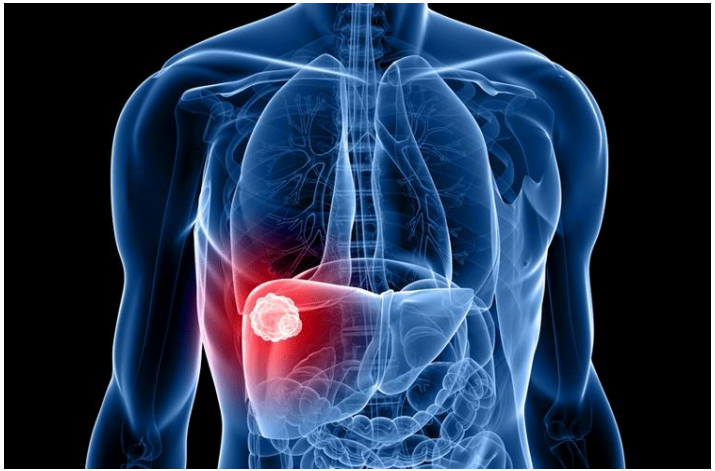


*** ~ 70% 1st line patients treated with IO based regimen**

Epidemiology data : Internal best current estimates of patient numbers based on external research

IPH5401 – COMMERCIAL OPPORTUNITY

HCC – OPTIMIZING IO RESPONSE



- **>500,000** people affected
- Third leading cause of cancer deaths
- Moderate activity of CPI

IO-naive patients

Advanced stage HCC*

1st line

US: 5k
EU5: 10k
Japan: 10k

25k Patients treated

2nd line

US: 5k
EU5: 5k
Japan:

13k Patients treated

*** IO likely to become the standard of care in 1st line**

Epidemiology data : Internal best current estimates of patient numbers based on external research

INNATE PHARMA – LONG TERM CATALYSTS

H1-2018	H2-2018	2019	2020	2021	2022	2023+	
Mona + Durva + CT Ph 1/2	Mona + Durva Ph2-SCCHN	**Mona potential pivotal program***					
		IPH4102 Pivotal-CTCL	IPH4102 Ph1/2-PTCL	**IPH4102 Pivotal-PTCL**			
	IPH5401 + Durva Ph1/2	IPH5401 + PD1/L1 Ph2-3rd indication	IPH43 Ph 1/2	**IPH5401 potential pivotal program***	IPH43 Ph 2/3	**IPH43 potential pivotal program***	
		IPH4102 Pivotal-SS	IPH4102 Ph 1/2 ATLL	**IPH4102 Pivotal-ATLL**			
			IPH52 Ph 1	IPH52 combo Ph 1/2		**IPH52 potential pivotal program***	
Mona + Cetux SCCHN	Mona + Cetux SCCHN update	Mona + Durva + CT Ph1/2	Mona + Durva Ph2-SCCHN	Mona potential pivotal program*	Mona Potential BLA*		
Mona + Durva*	Mona + Durva Other tumors*	Mona + Cetux Mona + Durva Update				IPH4102 Pivotal-ATLL	
	IPH4102 cohort expansion in SS		IPH4102 Pivotal - SS	IPH4102 SS Potential BLA*	IPH4102 Pivotal-CTCL	IPH4102 Pivotal-PTCL	IPH4102 CTCL, ATLL, PTCL Potential BLA*
		IPH5401 + Durva Ph1	IPH5401 + Durva Ph1/2	IPH43 Ph 1		IPH5401 potential pivotal program*	IPH5401 Potential BLA*
			IPH5401 + PD1/L1 Ph2-3rd indication	IPH52 Ph 1			IPH52 combination Ph 1/2

First Patient In

Data read out

Potential BLA

** Subject to data/governance decision*

UPCOMING CONFERENCE AACR 2018

INNATE PHARMA TO PRESENT NEW DATA FROM ITS IMMUNO-ONCOLOGY PORTFOLIO

- **Oral presentation of Eric Vivier**, CSO, on next generation immunotherapies
- **5 presentations by Innate Pharma teams**, including:
  - > Preliminary clinical efficacy data on monalizumab in combination with cetuximab in R/M SCCHN
  - > 2 posters on preclinical data supporting the rationale for the development of monalizumab in combination with cetuximab or durvalumab
  - > 1 poster on anti-CD39/anti-73 antibody programs targeting the adenosine pathway
  - > 1 poster on new antibody anti-Siglec-9
- Preclinical abstracts will be available on AACR website after March 14, 2018

QUESTIONS & ANSWERS

CLOSING REMARKS

MONDHER MAHJOUBI

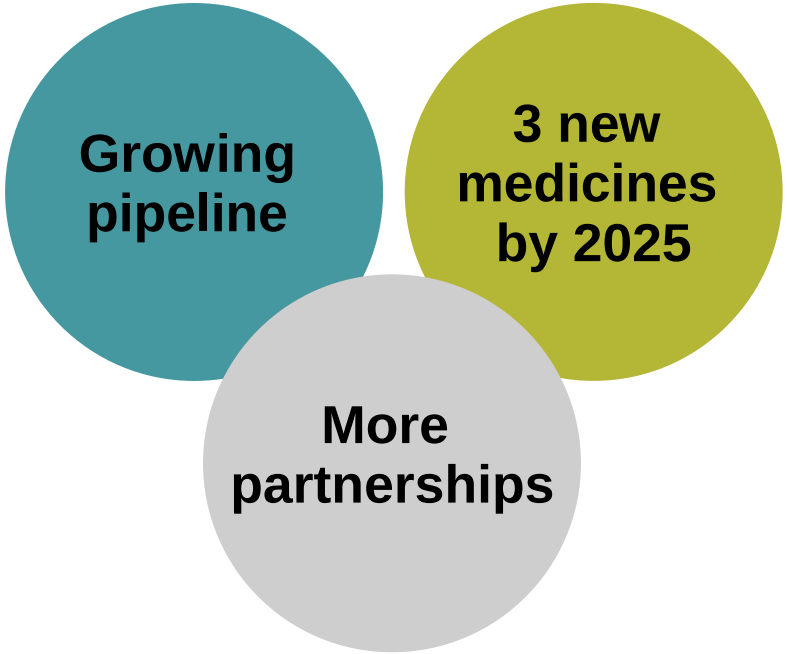
CHIEF EXECUTIVE OFFICER

KEY MESSAGES

- World-class science and technology platform
- Clinical read-outs ahead for monalizumab and IPH4102 programs
- Delivering on IPH5401 with clinical collaborations to accelerate development
- Potential to address large unmet medical needs in cancer
- Financial strength, enabling room for investment

INNATE PHARMA – OUR AMBITION

BUILDING IO LEADERSHIP



Disciplined execution

THE INNATE IMMUNITY **COMPANY**

innate pharma

THANK YOU

IPH
LISTED
EURONEXT

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Qualité
AFNOR CERTIFICATION