

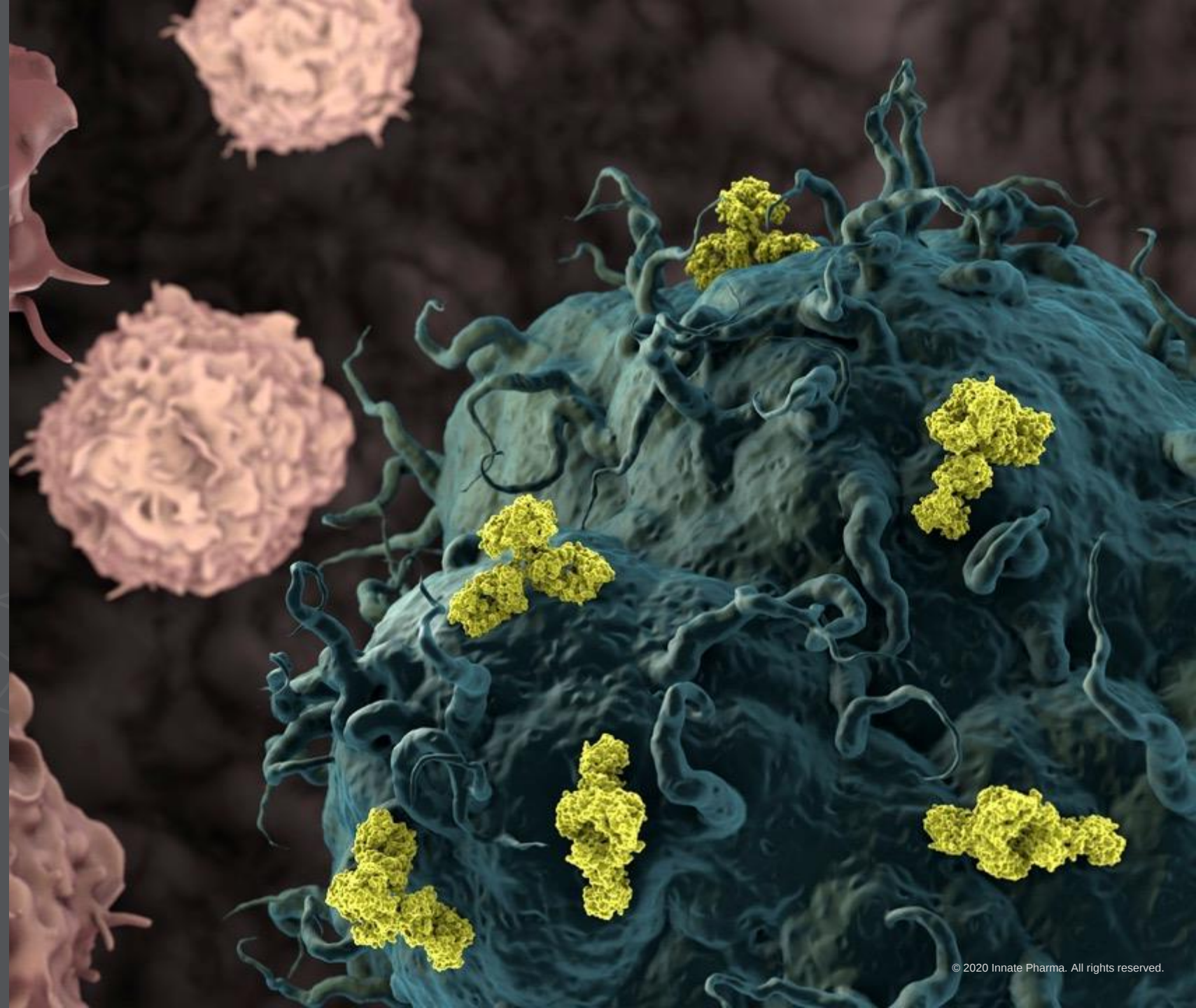


# Understanding the Potential of Lacutamab Across T Cell Lymphoma

February 9, 2021

PARIS: IPH.PA

NASDAQ: IPHA



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## Welcome & Introduction

*Mondher Mahjoubi, MD*

## Lacutamab Overview & Development Strategy

*Joyson Karakunnel, MD, MSc, FACP*

## Epidemiology & Unmet Need in CTCL & PTCL

*Pierluigi Porcu, MD*

## Collaboration with LYSA for PTCL

*Olivier Hermine, MD, PhD*

## Upcoming Catalysts & Concluding Remarks

*Joyson Karakunnel, MD, MSc, FACP & Mondher Mahjoubi, MD*

## Q&A

*All*

# Speakers on today's call



**Mondher Mahjoubi, MD**

*Chief Executive Officer*

*Chairman of the Executive Board*



**Joyson Karakunnel, MD, MSc, FACP**

*EVP, Chief Medical Officer*



**Pierluigi Porcu, MD**

*Professor of Medical Oncology, Dermatology and Cutaneous Biology*

*Director, Division of Hematologic Malignancies and Hematopoietic Stem Cell Transplantation at Thomas Jefferson University, US*

*Principal Investigator of Innate's Phase 2 TELLOMAK clinical trial*



**Olivier Hermine, MD, PhD**

*Professor of Hematology at the University of Paris Descartes*

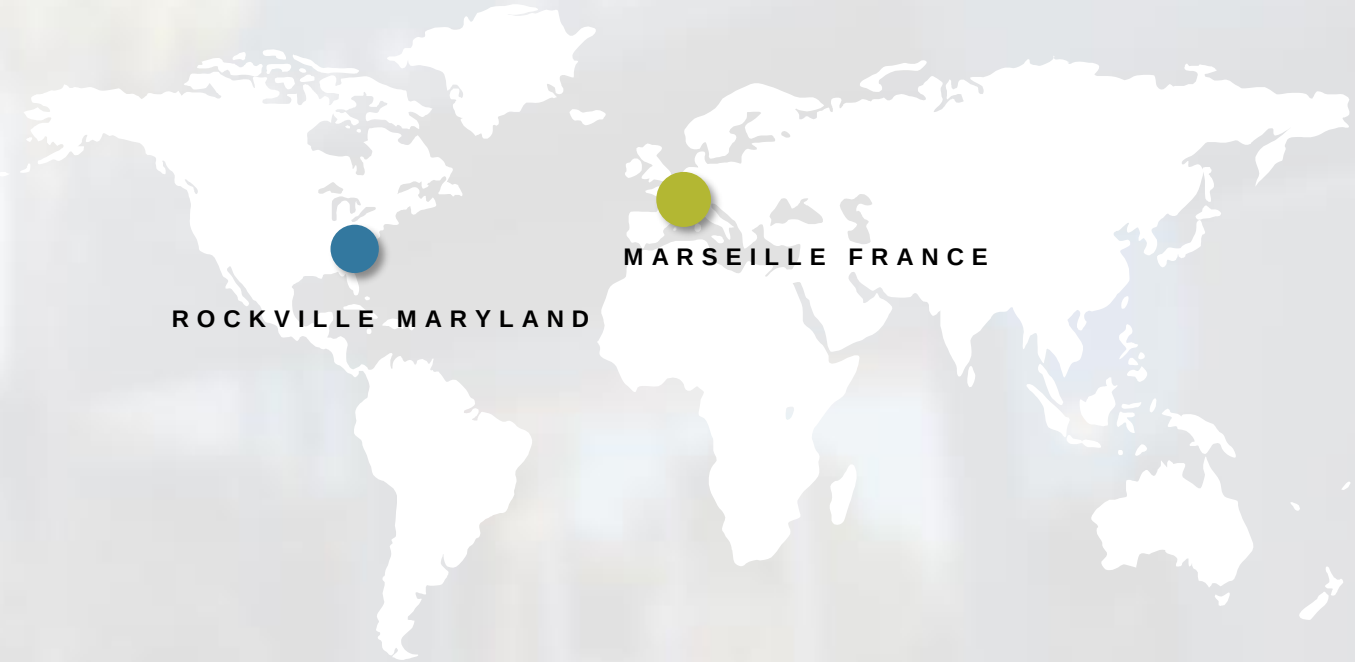
*Director, Division of Adult Hematology at Hôpital Universitaire Necker Enfants Malades*

*Member of the Académie des Sciences*

*Member of the Lymphoma Study Association (LYSA), France*

# A Leading Company in the Field of Innate Immunity

- Global, clinical-stage oncology-focused biotech company.
- Scientific excellence in the field of innate immunity with expertise in natural killer cell biology and antibody engineering.
- Focused pipeline of antibodies, including several potentially first-in-class clinical and preclinical candidates in cancers with high unmet medical need.



Founded: 1999

Paris Euronext listing: 2006

Nasdaq listing: 2019

# Scientific Innovation Drives Our Strategy

We aim to harness our scientific know-how in innate immunity and antibody engineering to develop oncology products that improve the lives of patients



**Drive near-term  
value with  
Lacutamab**



**Advance our  
innovative R&D  
pipeline**



**Build a  
sustainable  
business**

# Strong Science + Strong Partnerships = Robust Pipeline

**Validated  
Science**  
in high-impact  
publications



**Strong Track  
Record of  
Collaborations**  
with industry and  
academia



**Robust  
Pipeline**  
with innovative  
pre-clinical and  
clinical assets

THE LANCET  
Oncology  
nature Cell  
Science  
JOURNALS AAAS

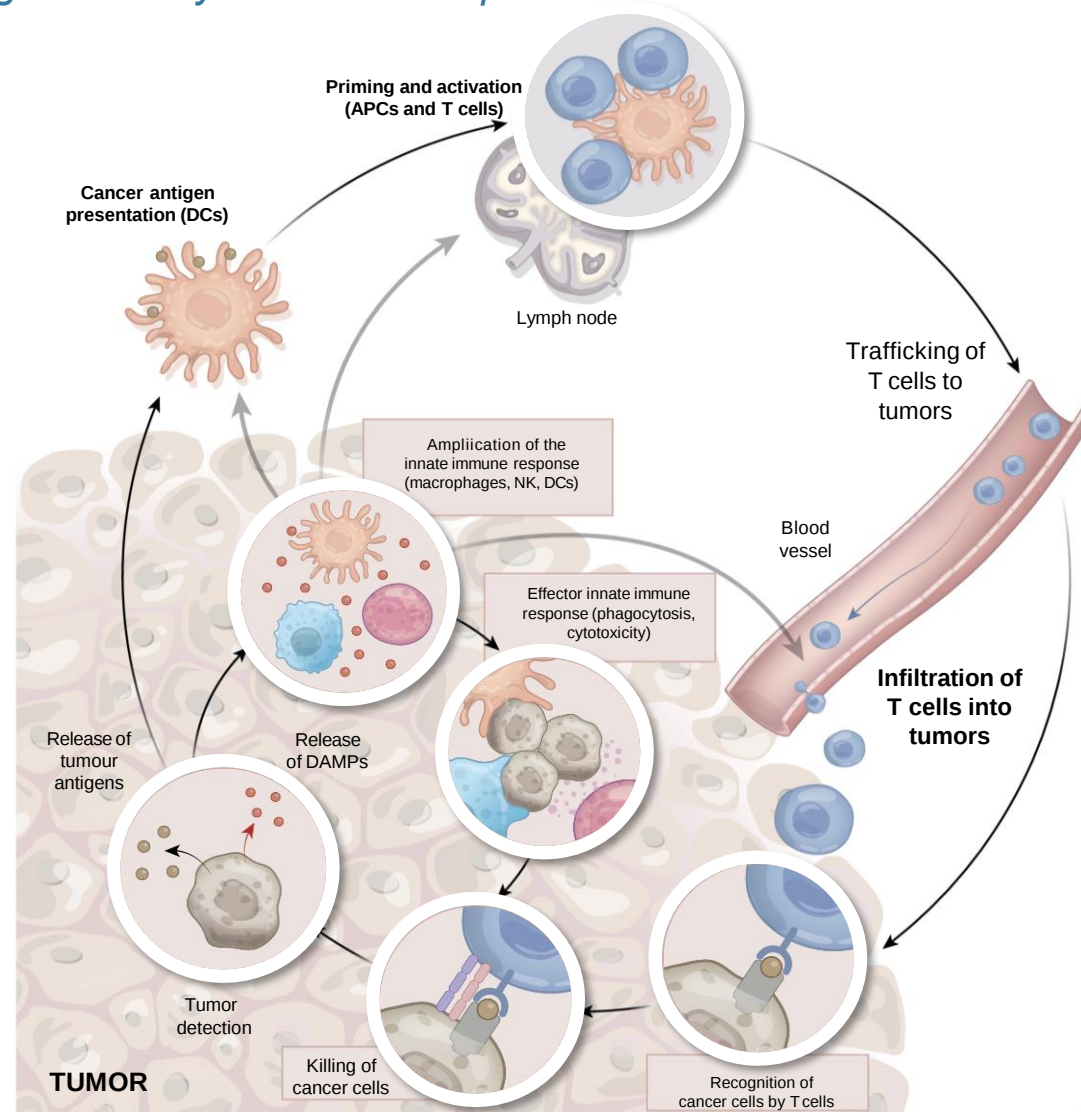


# Innate's Approach: Harnessing Innate Immunity in Cancer

*Choosing the right targets to leverage the body's immune response*

**2** **Unleash NK cells**  
Monalizumab (NKG2A)

**1** **Engage NK cells towards tumor**  
Lacutamab (KIR3DL2)  
NK cell engagers (NKp46)



**Reverse suppression**

IPH5201 (CD39)  
IPH5301 (CD73)

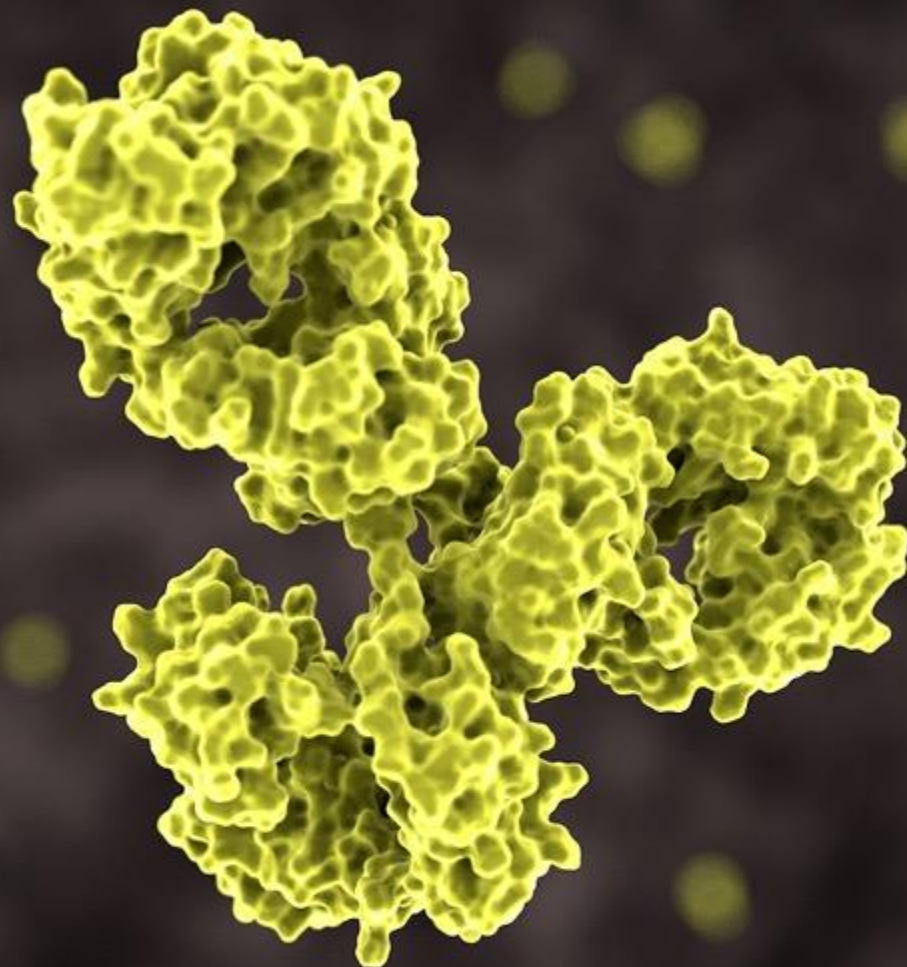
**3**

# Innate's Robust Pipeline Leveraging Expertise in Antibody Engineering & Innate Immunity Against Novel Cancer Targets



| Program                         | Target                                                                                                                              | Indication                                   | Pre-Clinical                                   | Phase 1 | Phase 2 | Phase 3 | Partner                    |
|---------------------------------|-------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------|------------------------------------------------|---------|---------|---------|----------------------------|
| <b>Lacutamab</b><br>(IPH4102)   | KIR3DL2                                                                                                                             | Sézary Syndrome                              | PHASE 2 (FDA FAST TRACK/EMA PRIME DESIGNATION) |         |         |         | —                          |
|                                 |                                                                                                                                     | Mycosis Fungoides                            | PHASE 2                                        |         |         |         | —                          |
| <b>Monalizumab</b>              | NKG2A                                                                                                                               | Squamous Cell Carcinoma of the Head and Neck | PHASE 3                                        |         |         |         | AstraZeneca                |
|                                 |                                                                                                                                     | Solid Tumors (including CRC and NSCLC)       | PHASE 1/2                                      |         |         |         |                            |
| <b>Avdoralimab</b><br>(IPH5401) | C5aR                                                                                                                                | Bullous pemphigoid                           | PHASE 2                                        |         |         |         | —                          |
|                                 |                                                                                                                                     | COVID-19                                     | PHASE 2                                        |         |         |         | —                          |
| <b>IPH5201</b>                  | CD39                                                                                                                                | Cancer (solid tumors)                        | PHASE 1                                        |         |         |         | AstraZeneca                |
| <b>Preclinical portfolio</b>    | IPH5301 (CD73), IPH6101**(NKCE)<br>IPH25*, IPH26* (siglec-9), IPH43* (MICA/B), IPH62* (NKCE),<br>IPH64**(NKCE), IPH45, IPH65 (NKCE) |                                              | PC                                             |         |         |         | * AstraZeneca<br>** SANOFI |

"CRC" = Colorectal Cancer; "NSCLC" = Non-Small Cell Lung Cancer



# Lacutamab Overview & Development Strategy

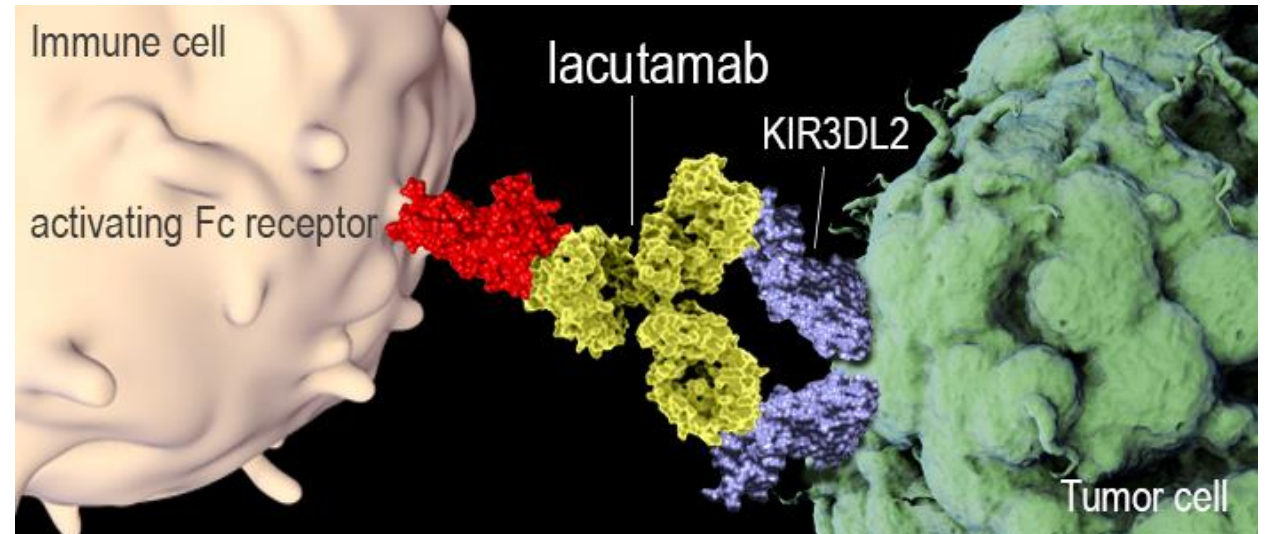
Joyson Karakunnel, MD, CMO



# Lacutamab: Lead Proprietary Asset

## First-in-class anti-KIR3DL2 humanized cytotoxicity-inducing antibody

- Lacutamab under development for the treatment of various forms of T-cell lymphomas (TCL)
- Compelling Phase 1 data in Sézary syndrome (SS), published in *Lancet Oncology*
- EMA PRIME and FDA Fast Track designations for SS patients who have received at least two prior systemic therapies
- Orphan drug designation in the EU and US for the treatment of cutaneous TCL (CTCL)
- Development strategy:
  - Fast to market strategy in SS
  - Expansion in other forms of T-cell lymphomas: mycosis fungoides (MF) and peripheral T-cell lymphoma (PTCL)



# Development Informed by Target Expression

## KIR3DL2 EXPRESSION

## INCIDENCE *Major markets (US, EU5, Japan), 2025*

### SEZARY SYNDROME

- >90% of patients express target\*
- All tissues involved (skin, blood and lymph nodes)

~80–200 patients<sup>1</sup>

### MYCOSIS FUNGOIDES

- ~50% of patients express target\*

2,200–4,000 patients<sup>1</sup>

### PERIPHERAL T-CELL LYMPHOMA

- KIR3DL2 is expressed in multiple PTCL subtypes
- ~50% of patients express target\*

~18,000 patients<sup>2</sup>

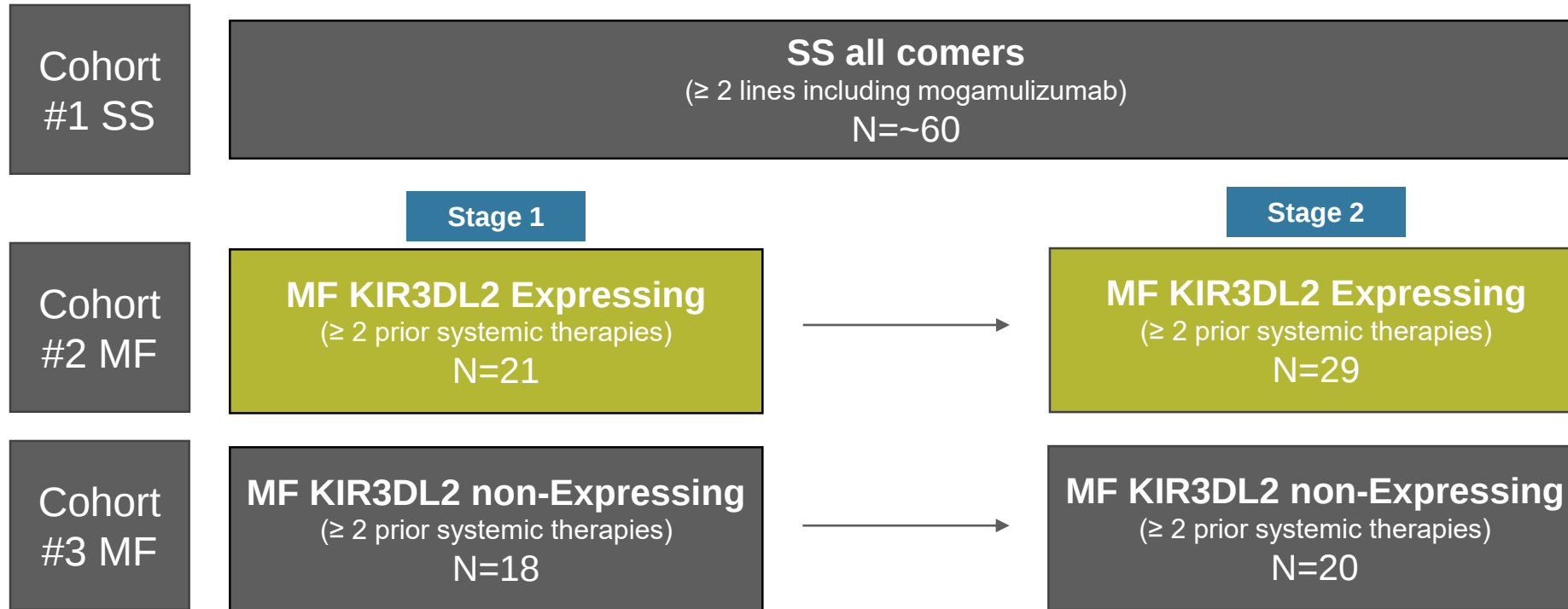
SS: Roelens, M. et al. (2019); MF: Battistella, Blood 2017; PTCL: M. Cheminant et al, ICML-15 2019

\*Target expression is defined by % of KIR3DL2-expressing tumor cells > 1%

1. SS and MF: SEER Incidence Rates and Annual Percent Change by Age at Diagnosis — All Races, Both Sexes, 2008-2017; SEER Cancer Statistics Review 1975-2017; -- Dobos, G. et al. (2020)

2. PTCL: Delve Insights MR Report

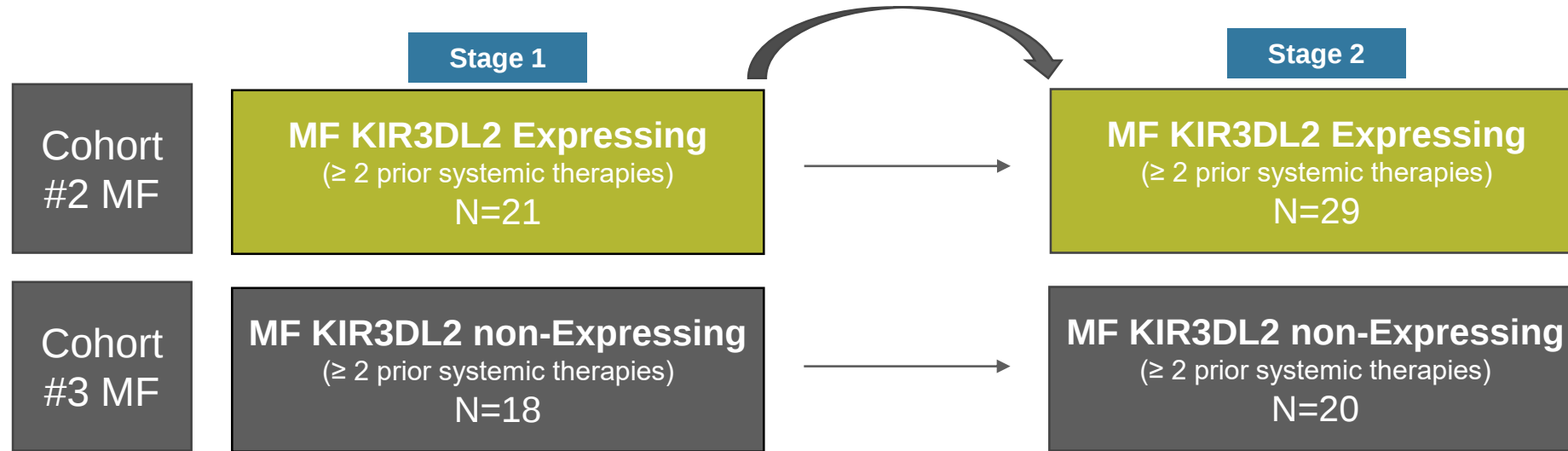
# Phase 2 TELLOMAK Study Evaluating Lacutamab Across Subtypes of CTCL



## STUDY ENDPOINTS

- Primary endpoint: objective response rate
- Key secondary endpoints: progression-free survival, duration of response, quality of life and adverse events

# Early Signals in KIR3DL2-Expressing MF Support Advancing Cohort 2 into Stage 2 of TELLOMAK



Cohort 2 moves to stage 2 after predetermined number of responses was reached

## NOW

### RELAPSE SETTING

**Highest unmet medical need;  
two-pronged approach:**

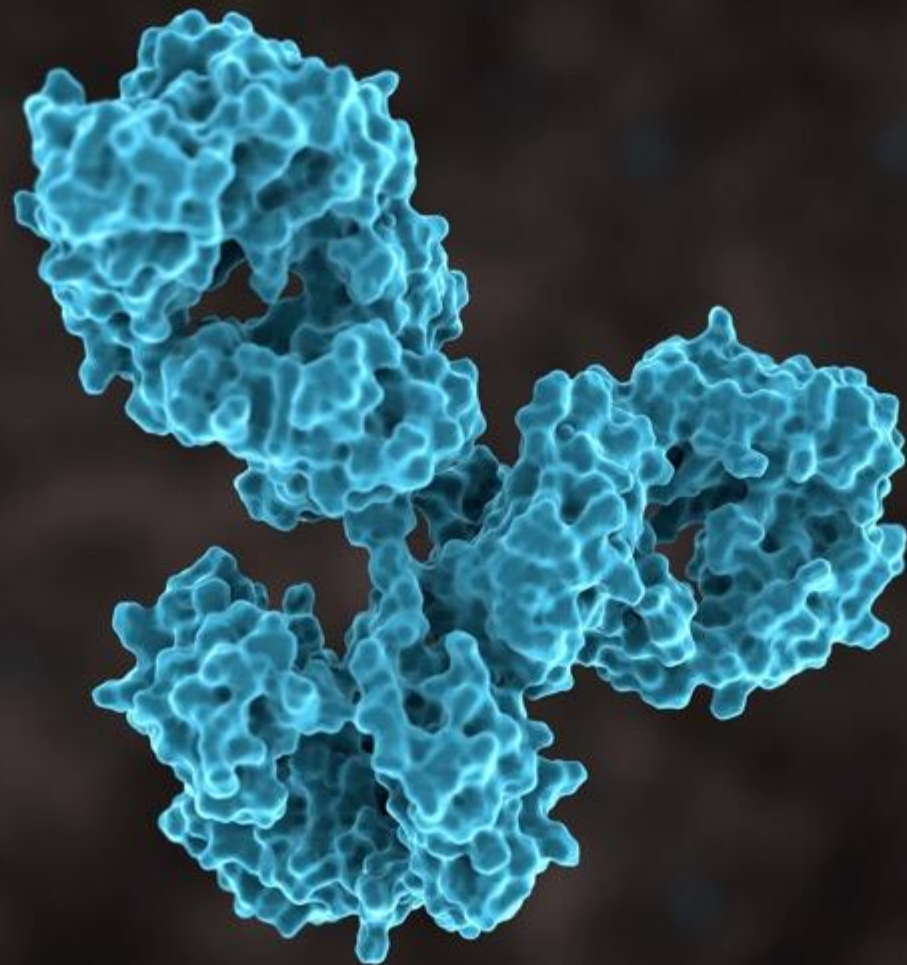
- Single agent activity (monotherapy)
- Combination studies with: 1) GemOx and 2) other SOC

## NEXT STEPS

### FRONTLINE

**Driven by data in relapse setting  
to advance into earlier lines**

- Combination with CHOP



## Pierluigi Porcu, MD

*Professor of Medical Oncology, Dermatology and Cutaneous Biology*

*Director, Division of Hematologic Malignancies and Hematopoietic Stem Cell Transplantation at Thomas Jefferson University, US*

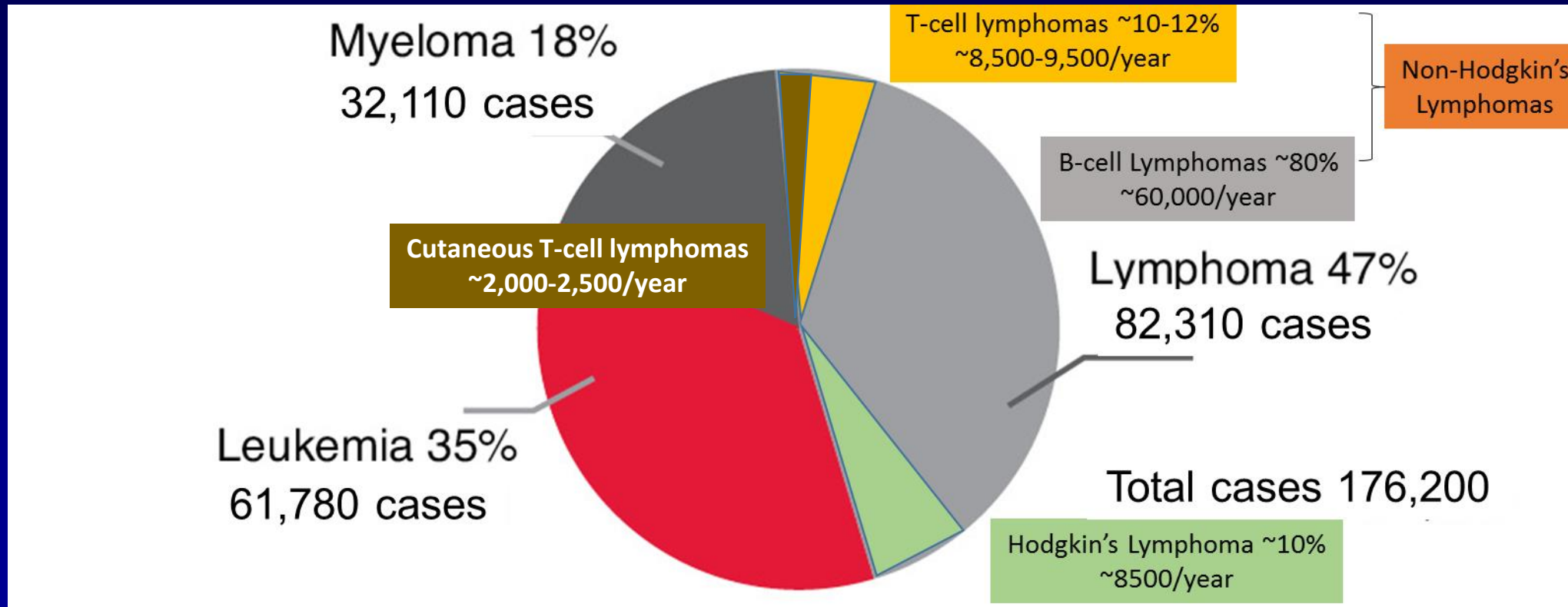
*Principal Investigator of Innate's Phase 2 TELLOMAK clinical trial*



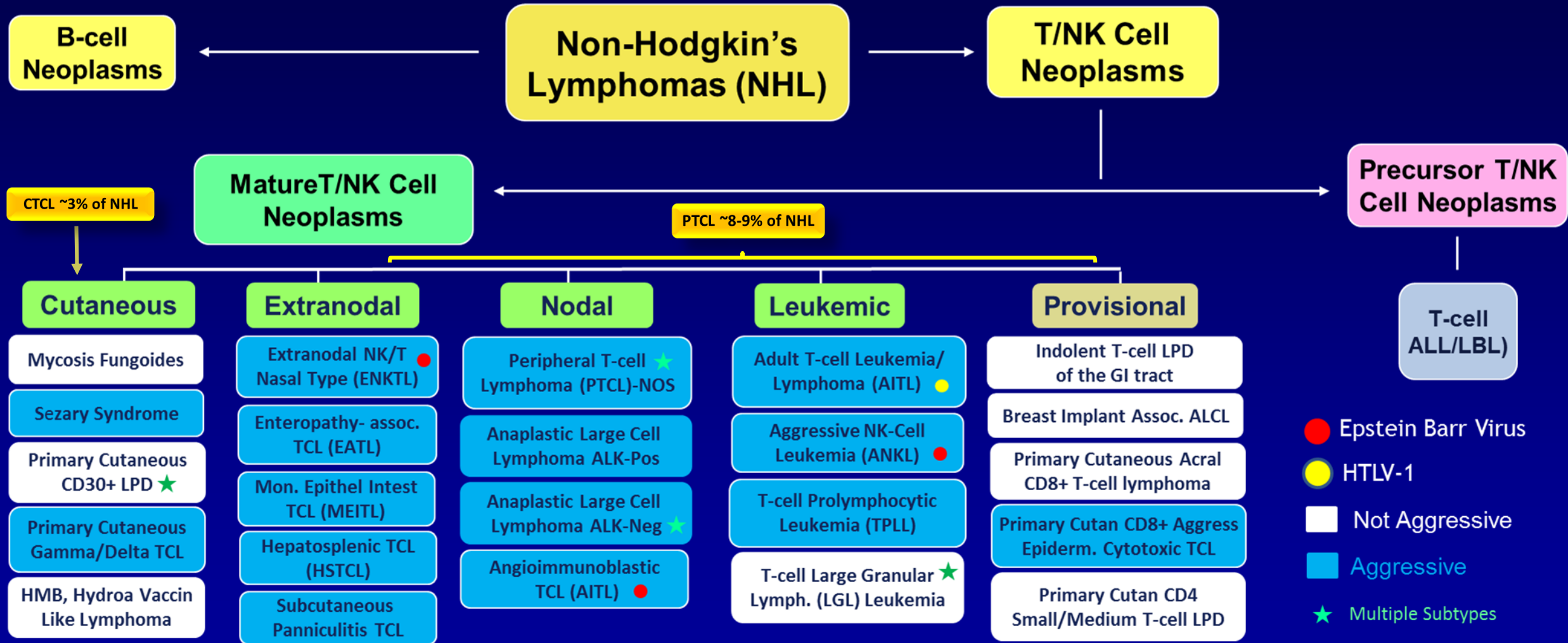
# **T-cell Lymphomas**

## **Epidemiology, disease spectrum, and clinical unmet need**

# Estimated New Cases (%) of Leukemia, Lymphoma, and Myeloma in the US, 2019



# WHO 2016 Classification of T-Cell Neoplasms



# Cutaneous T-cell Lymphomas

# CTCL Incidence Varies by Subtype, Subtypes Difficult to Diagnose

- CTCLs are heterogenous hematologic neoplasms of skin-homing, mature T cells
- Initially skin-limited, they can involve visceral organs, lymph nodes, and blood<sup>1,2</sup>
- Annual incidence rate of CTCL ~0.5 per 100,000 people<sup>3</sup> (~3,000/year); Estimated prevalence ~25-30,000 cases/year<sup>4</sup>
- Median age at diagnosis: 55-60 years
- Average time from disease onset to diagnosis: 6 years <sup>3</sup>

| Variable                                 | Geo.             | % SS            | % MF             | % Oth. CTCL        |
|------------------------------------------|------------------|-----------------|------------------|--------------------|
| Subtype Split:<br>Most likely<br>[Range] | US <sup>1</sup>  | 1%<br>[1%-2%]   | 56%<br>[53%-59%] | 43%<br>[39%-46%]   |
|                                          | 5EU <sup>2</sup> | 4%<br>[3%-6%]   | 62%<br>[57%-68%] | 34%<br>[26%-40%]   |
|                                          | JP <sup>3</sup>  | 1.5%<br>[1%-2%] | 63%<br>[45%-65%] | 35.5%<br>[33%-54%] |

<sup>1</sup> Meta-analysis ranges specific to region is used; -- Dobos, G. et al. (2020) [Meta-analysis with regional estimates]; Bradford, P. T. et al. (2009) [similar proportions, 1.2% SS; 53.75% MF]

<sup>2</sup> Meta-analysis ranges specific to region is used -- Dobos, G. et al. (2020)

<sup>3</sup> Based on Meta-Analysis covering Asian Population [2,187 CTCL Patients] and most recent Japanese Study -- Dobos, G. et al. (2020); K. Fujii et al. (2020) [Data for 2012-2017, N=2090 CTCL, CBCL]; Hamada, T., et al. (2014)

| CTCL Subtype<br>(WHO-EORTC Classification 2018) <sup>2</sup>                                         | 5-Year Survival     |
|------------------------------------------------------------------------------------------------------|---------------------|
| Mycosis fungoides (MF)                                                                               | 88%                 |
| Mycosis fungoides variants<br>Folliculotropic MF<br>Pagetoid reticulosis<br>Granulomatous slack skin | 75%<br>100%<br>100% |
| Sézary syndrome (SS)                                                                                 | 36%                 |
| Primary cutaneous CD30+ LPDs<br>C-ALCL<br>LyP                                                        | 95%<br>99%          |
| Subcutaneous panniculitis-like TCL                                                                   | 87%                 |
| Primary cutaneous g/d T-cell lymphoma                                                                | 11%                 |
| Primary cutaneous PTCL, NOS                                                                          | 15%                 |

<sup>a</sup> **OTHER** is groups with <1% each, and include additional MF variants; ATL; extranodal NKTCL, nasal type; primary cutaneous g/d TCL, CD8+ AECTCL (provisional), and others. AECTCL, aggressive epidermotropic CTCL; cALCL, cutaneous ALCL; EORTC, European Organization for Research and Treatment of Cancer; LPD, lymphoproliferative disease; LyP, lymphomatoid papulosis; <sup>4</sup>Data from: Cutaneous Lymphoma Foundation

# Mycosis Fungoides: A low grade CD4+ T-cell lymphoma

Normal or  
Near normal

Immune Competence

Impaired

## 1. A state of dynamic but stable equilibrium

- Evolving (pre)malignant T-cell clone(s)
- Near normal immune system

## 2. A state of dynamic and unstable equilibrium

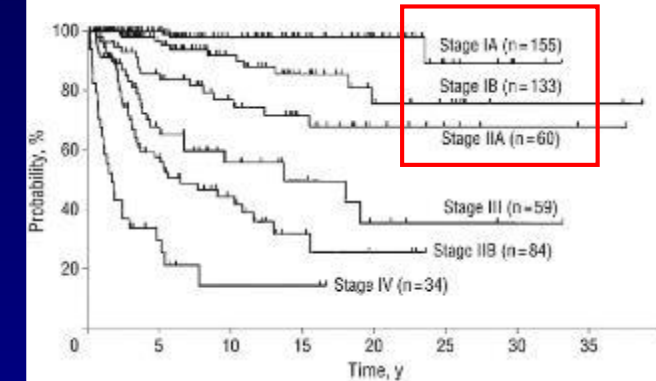
- Evolving malignant T-cell clone
- Defective immune system

## 3. A population of highly mutated malignant T-cells with

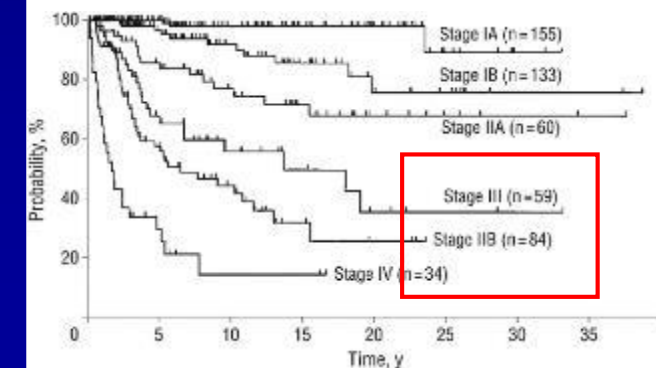
- Vertical, nodular growth
- Aberrant trafficking
- Defective apoptosis
- Progression and death



Disease specific survival for  
early stage (IA, IB, IIA) MF



Disease specific survival for  
advanced stage (IIB, III, IV) MF

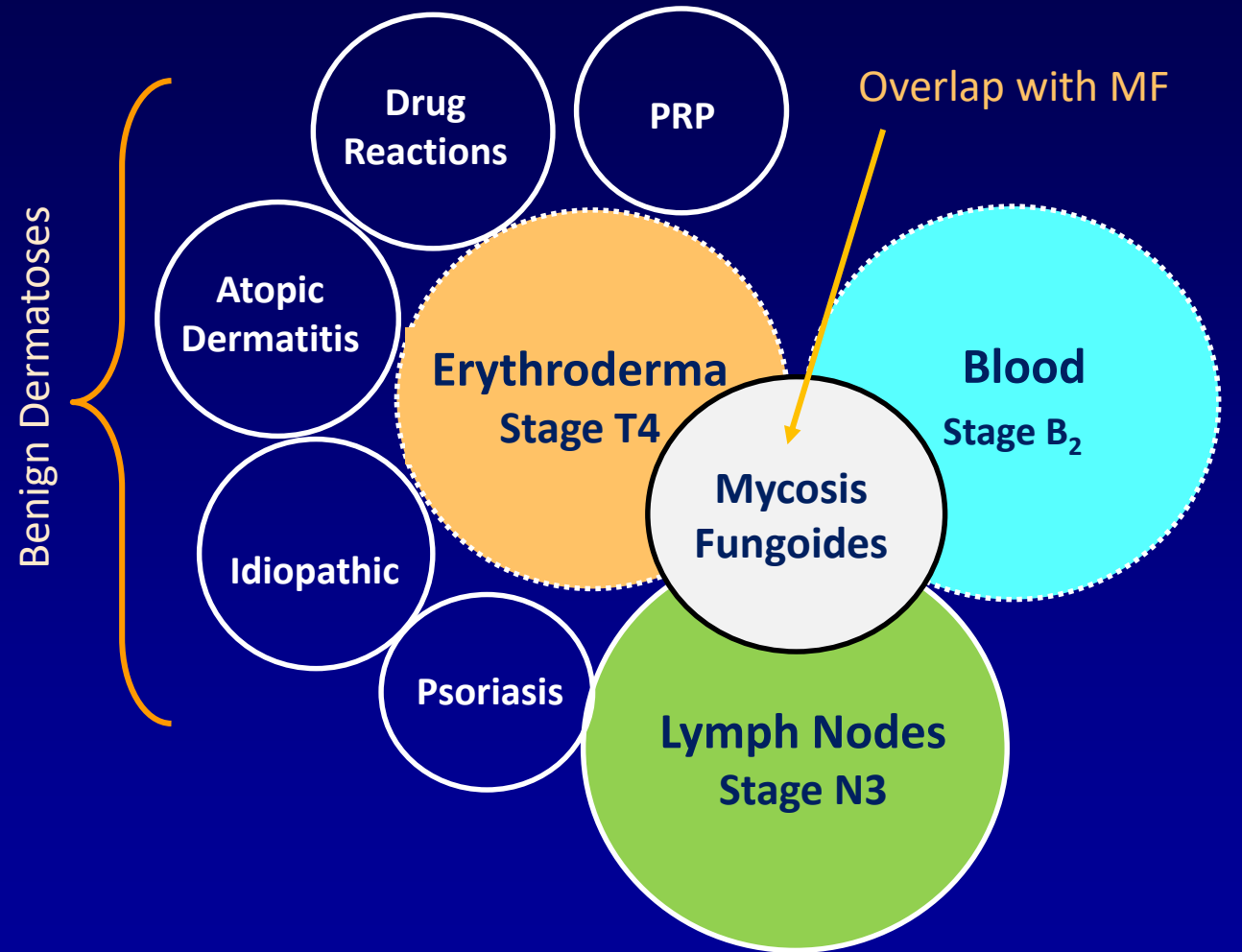
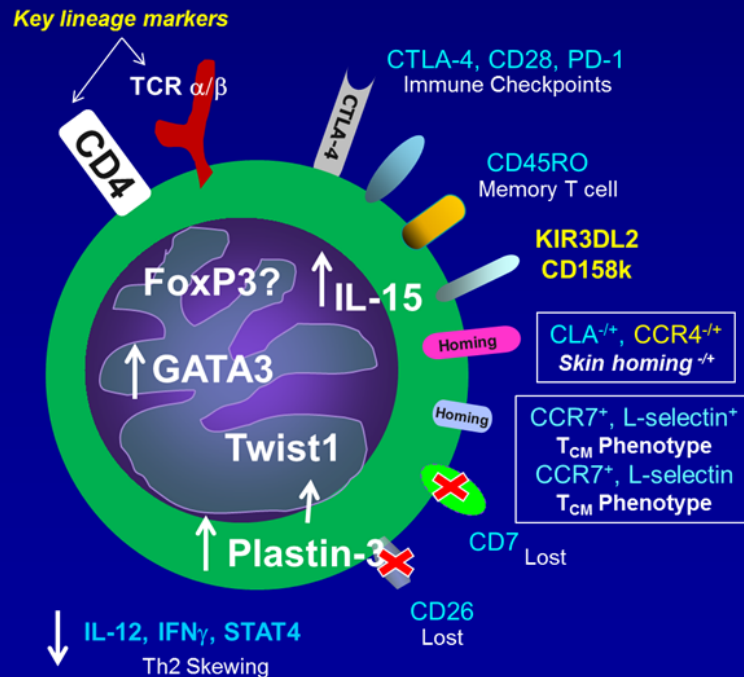


# What is Sezary Syndrome?

Three clinical elements to determine response in SS

1. Erythroderma (*Skin*)
2. Circulating Tumor Cells (*Blood*)
3. Lymphadenopathy (*Lymph Nodes*)

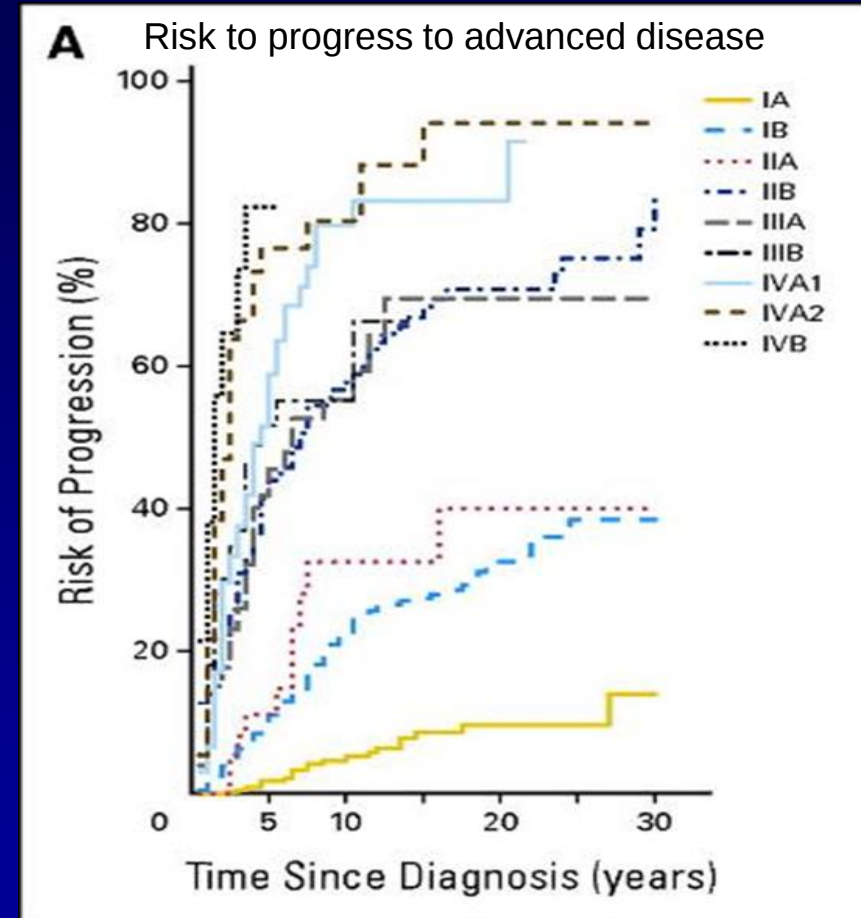
Sezary Cell Biomarkers



Pierluigi Porcu, MD

# Management of CTCL and Risk for Progression

- MF is immunologically responsive
- Multiple therapies necessary over disease course
- Although FDA has approved multiple therapies, there is a high unmet need because most patients progress
- Stable Disease is a meaningful endpoint because provides relief of pruritus and skin symptoms
- 2/3 of the patients are at early stage while 1/3 are at an advanced stage of disease
- All patients will eventually need systemic therapies
- Median survival in advanced stages ranges from 1.5-3.5 years



Kim et al. Arch Dermatol. 2003;139:857

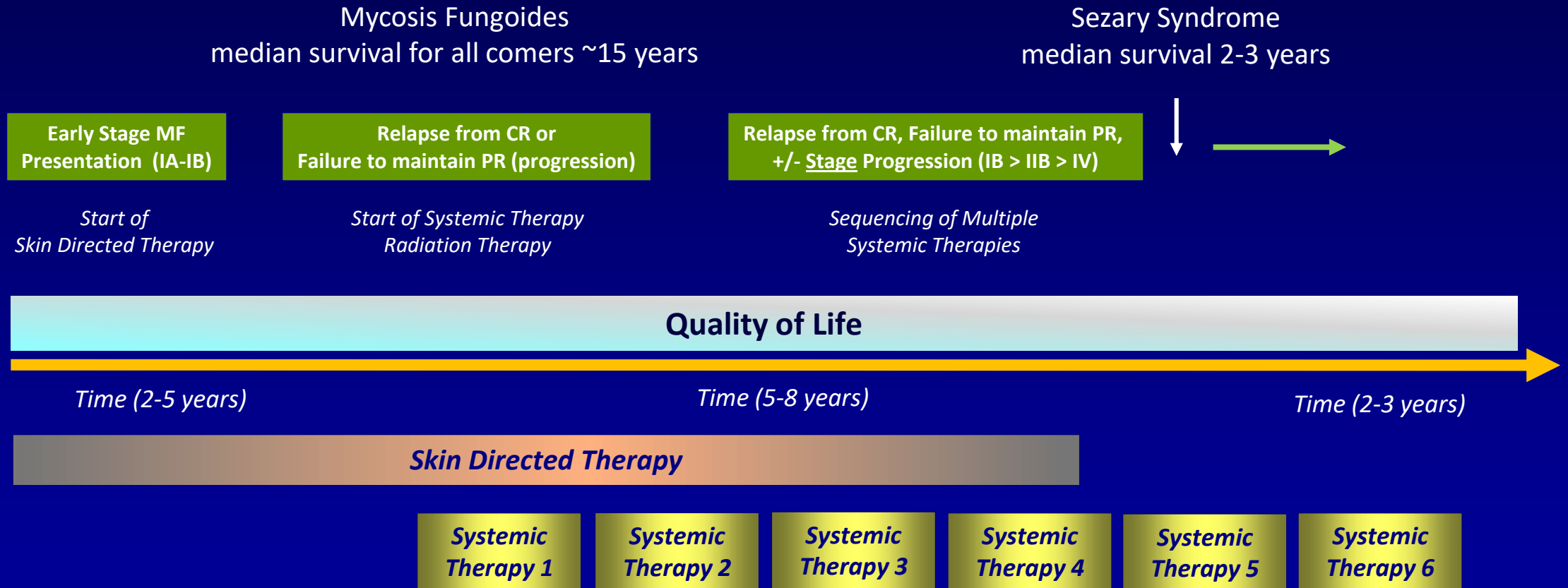
Agar et al. JCO 2010;28:4730-4739

Quaglino et al. Cancer 2012

Kim Y et al, Arch Dermatol 1999

Pierluigi Porcu, MD

# Natural Course of MF – Indolent but progressive, lifelong poor QoL, multiple sequential therapies, not curable



# Six Systemic Agents are Approved for CTCL Treatment

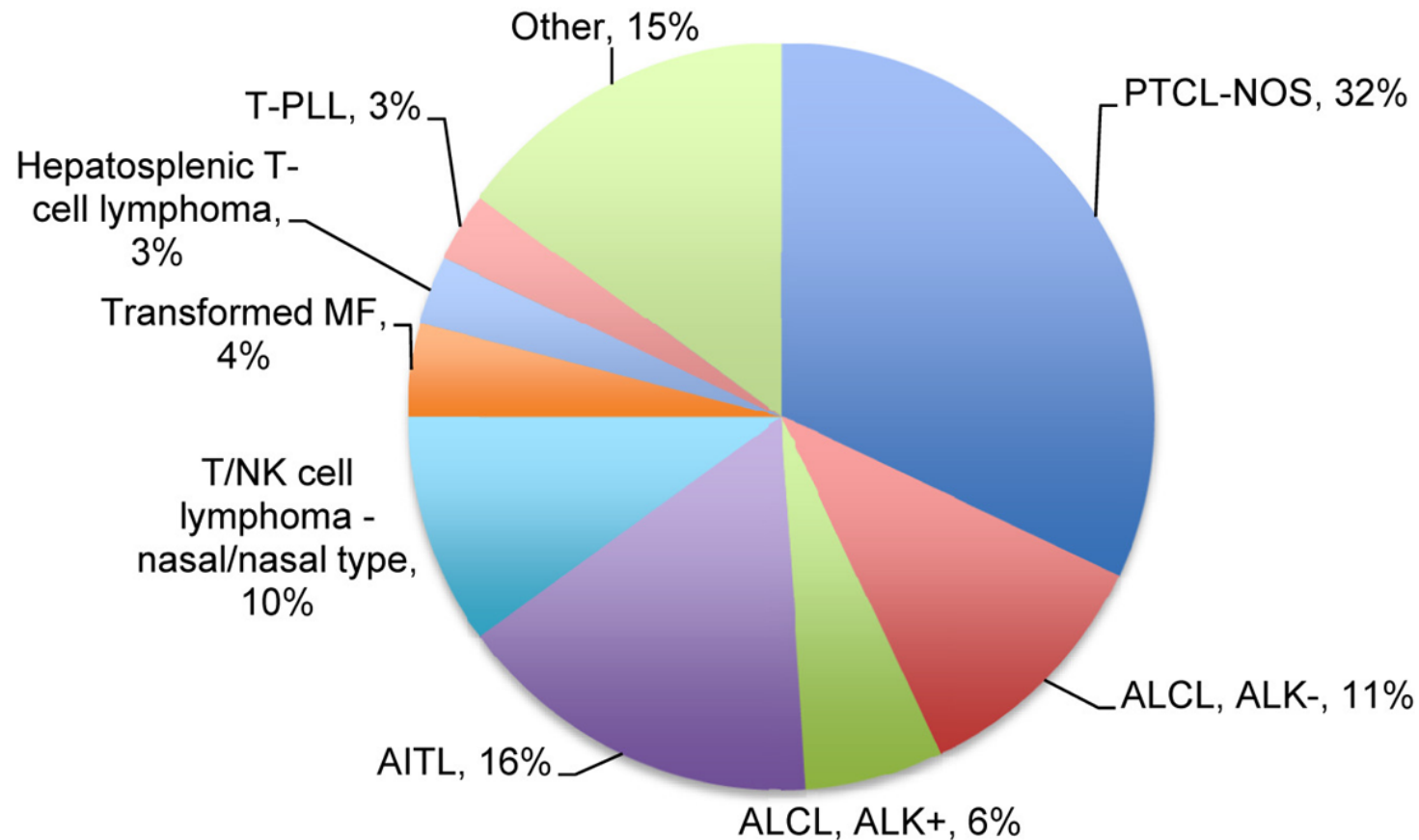
| Therapy                                             | MOA                               | Approval | Indication                                                                                     | ORR% (year)                       |
|-----------------------------------------------------|-----------------------------------|----------|------------------------------------------------------------------------------------------------|-----------------------------------|
| <b>Bexarotene (Targretin®)</b> <sup>1, 2</sup>      | Retinoid X agonist                | FDA/EMA  | Cutaneous lesions in patients with CTCL refractory to ≥ 1 prior systemic therapy               | 32% (2001)<br>15.8% (2017)        |
| <b>Vorinostat (Zolinza®)</b> <sup>3, 4</sup>        | HDAC Inhibitor                    | FDA      | Persistent/recurrent CTCL with cutaneous manifestations on or after 2 prior systemic therapies | 30% (2007)<br>5% (2018 - MAVORIC) |
| <b>Ontak (Denileukin diftitox®)</b> <sup>5</sup>    | Anti-CD25 Cytotoxin               | FDA/EMA  | Resistant/recurrent CTCL with cells that express CD25                                          | 30% (2001)                        |
| <b>Romidepsin (Istodax®)</b> <sup>6</sup>           | HDAC inhibitor                    | FDA      | CTCL with ≥ 1 prior systemic therapy                                                           | 34% (2010)                        |
| <b>Brentuximab vedotin (Adcetris®)</b> <sup>2</sup> | Anti-CD30 antibody-drug conjugate | FDA/EMA  | CD30+ CTCL after prior systemic therapy                                                        | 67% (2017)                        |
| <b>Mogamulizumab (Poteligeo®)</b> <sup>4</sup>      | Anti-CCR4 monoclonal antibody     | FDA.EMA  | R/R MF/SS after ≥ 1 systemic therapy                                                           | 28% (2018 - MAVORIC)              |

# Systemic Treatment Options in CTCL

|                            | <b>Mycosis fungoides</b>                                     | <b>Sézary syndrome</b>       |
|----------------------------|--------------------------------------------------------------|------------------------------|
| <b>1<sup>st</sup> line</b> | Bexarotene, bexarotene-based combinations                    | ECP, Bexarotene + interferon |
| <b>2<sup>nd</sup> line</b> | Brentuximab / Mogamulizumab                                  | Mogamulizumab                |
| <b>3<sup>rd</sup> line</b> | Romidepsin / vorinostat ^                                    |                              |
| <b>4<sup>th</sup> line</b> | Interferon, methotrexate, gemcitabine, liposomal-doxorubicin |                              |

# Peripheral T-cell Lymphomas

# COMPLETE Registry: Distribution of Diagnoses



A total of 499 patients were enrolled in the COMPLETE study from 40 academic centers and 15 community-based centers. Most (89%) of the patients were enrolled from academic centers. Excisional lymph node biopsy was performed most often (79% of patients), followed by core needle biopsy (14%) and fine needle aspiration (7%). Skin lesions were biopsied in 20% of the patients. The subtypes of reported PTCL or NK-cell lymphomas are shown. Consistent with other data,<sup>5, 6</sup> the 3 most common histologic types were PTCL, not otherwise specified (NOS), anaplastic large cell lymphoma (ALCL), both ALK-positive (ALK+) and ALK-negative (ALK-), and angioimmunoblastic T-cell lymphoma (AITL).

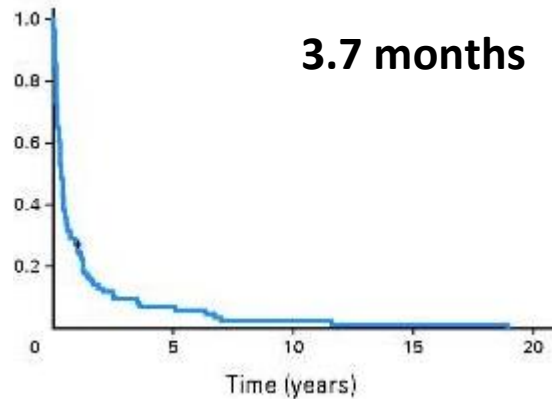
Hsi ED, Horwitz SM, Carson KR, et al. Analysis of Peripheral T-cell Lymphoma Diagnostic Workup in the United States. Clin Lymphoma Myeloma Leuk. 2017 Apr;17(4):193-200

**Pierluigi Porcu, MD**

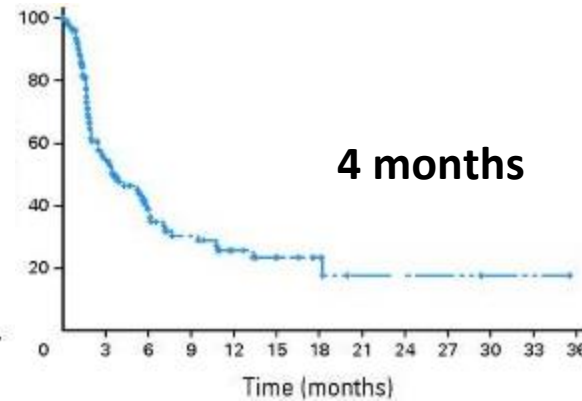
Subtypes vary in geographic distribution and outcome

# Progression Free Survival (PFS): Relapsed/Refractory PTCL

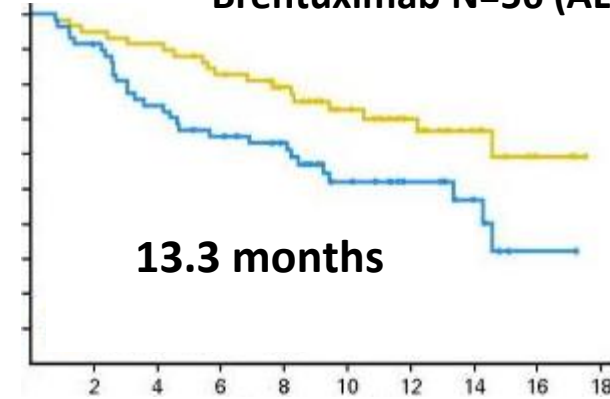
BCCA N=153



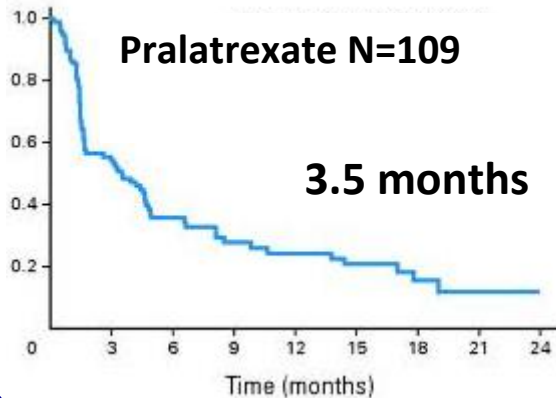
Romidepsin N=130



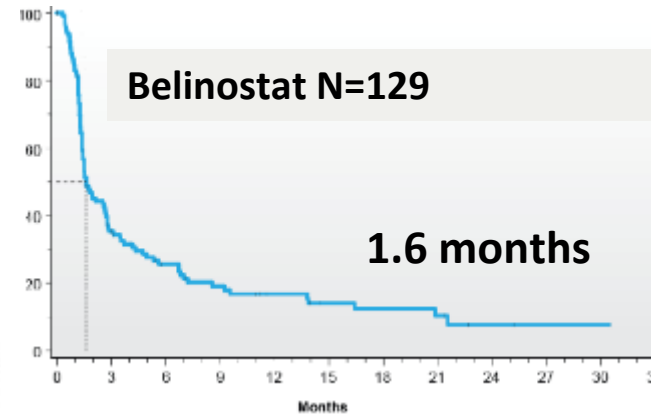
Brentuximab N=56 (ALCL)



Pralatrexate N=109

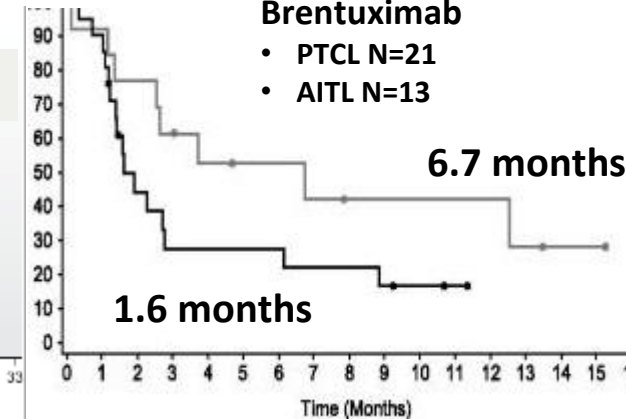


Belinostat N=129



Brentuximab

- PTCL N=21
- AITL N=13



BV now approved  
in front line  
setting for CD30+  
PTCL (US) and  
CD30+ ALCL (EU),  
thus no longer an  
option in R/R  
disease

# PTCL: Current “SOC”

1<sup>st</sup> line

2<sup>nd</sup> line

≥ 3<sup>rd</sup> line

|                                       |                 |                                                                                                                                                                                 |
|---------------------------------------|-----------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| CD30 expressing<br>~40% (mostly ALCL) | Brentuximab CHP | Combination chemotherapy<br>(e.g. GemOx, DHAP)<br><br>Romidepsin (FDA approved)<br>Pralatrexate (FDA approved)<br>Belinostat (FDA approved)<br>Single agent chemo (Gemcitabine) |
| CD30 non-expressing<br>~60%           | CHOP-like chemo |                                                                                                                                                                                 |

ORR

CD30+  
CD30-

~80%  
~70%

PFS

CD30+  
CD30-

~48mo  
~20mo

~30-45%  
~30-45%

~3-4mo  
~3-4mo

**High unmet need**

# Relapsed/Refractory PTCL: Current Treatment Overview

- Frontline therapy for PTCLs produces good response rates, including complete response rates, but fails to induce durable remission in most patients
- With the exception of ALCL (Brentuximab vedotin), there is no consensus salvage therapy for patients with relapsed/refractory PTCL and limited evidence for selective efficacy in PTCL subtypes
- Current second line and beyond therapies have only modest activity with a low CR rate
- Despite a number of FDA-approved agents, prognosis remains poor

# Targeting KIR3DL2 in TCL

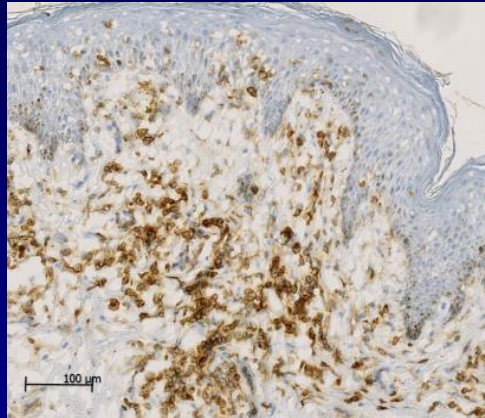
# Role of KIR3DL2 in CTCL

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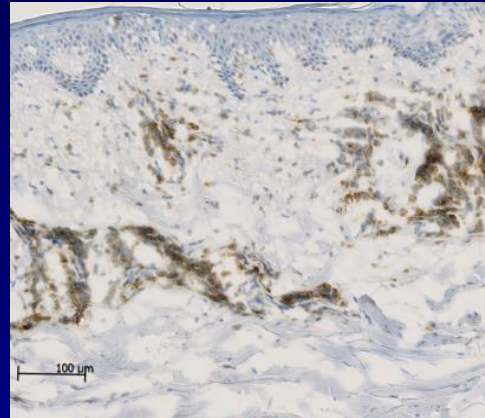
- KIR3DL2 is a member of the highly polymorphic family of killer-cell immunoglobulin-like receptors.
- It is expressed on subsets of normal T and NK cells but widely expressed in most subtypes of T-cell lymphoma.
- It is proposed as a the most sensitive diagnostic and prognostic marker for Sezary Syndrome (Hurabielle C et al; Clin Cancer Res 2017). It is also proven useful of follow-up (Bouaziz JD et al; Br J Dermatol 2010)
- In patients with CTCL, high expression is associated with advanced stage, presence of extra-cutaneous involvement and shorter overall survival

# KIR3DL2 expression in CTCL, according to WHO-EORTC subtype

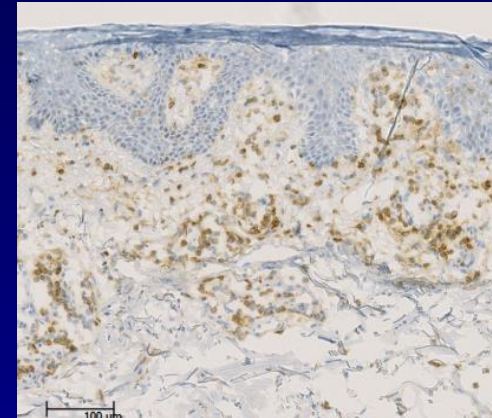
Sézary pt #1  
86.5% KIR3DL2+ tumor cells



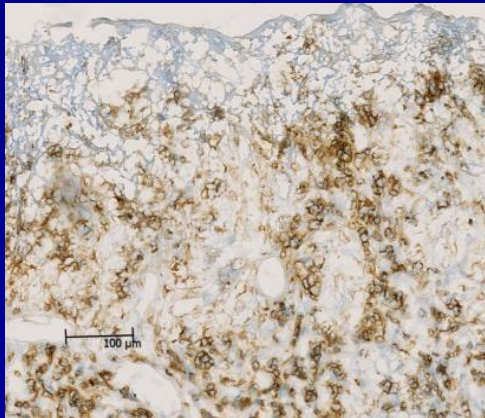
Sézary pt #2  
75.5% KIR3DL2+ tumor cells



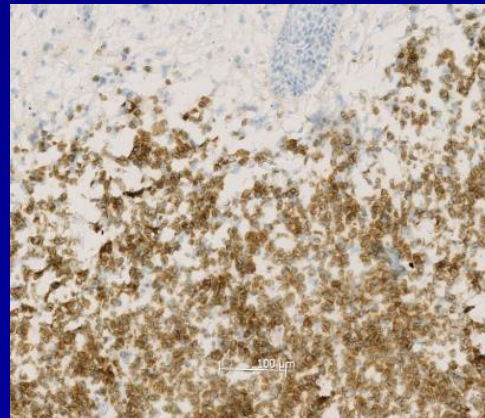
Sézary pt #3  
77.5% KIR3DL2+ tumor cells



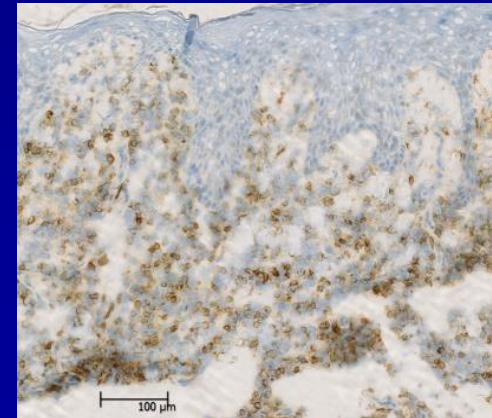
tMF pt #1  
88% KIR3DL2+ tumor cells



tMF pt #2  
96% KIR3DL2+ tumor cells

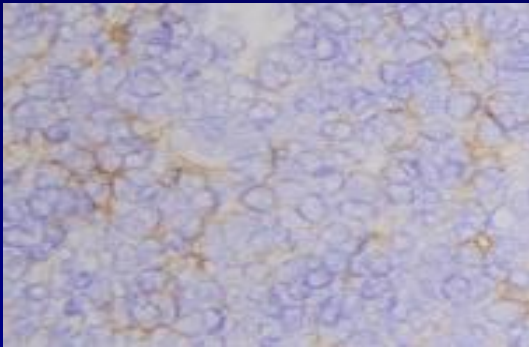


tMF pt #3  
83% KIR3DL2+ tumor cells

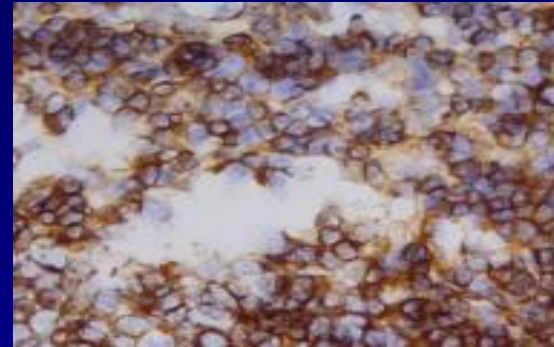
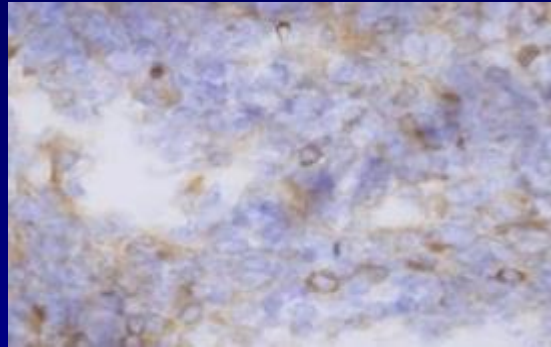


# KIR3DL2 expression in PTCL (Innate Pharma proprietary IHC test)

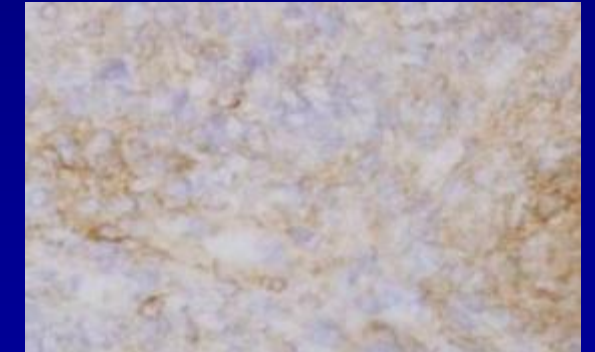
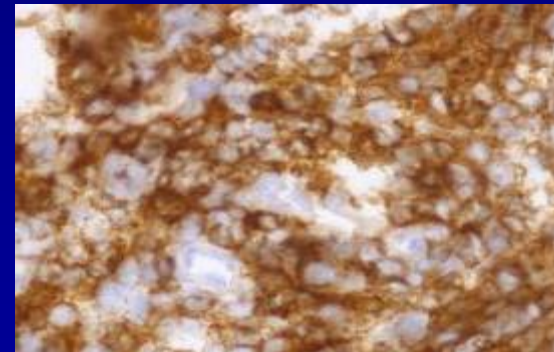
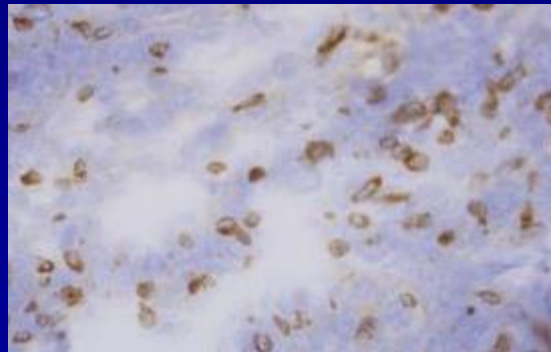
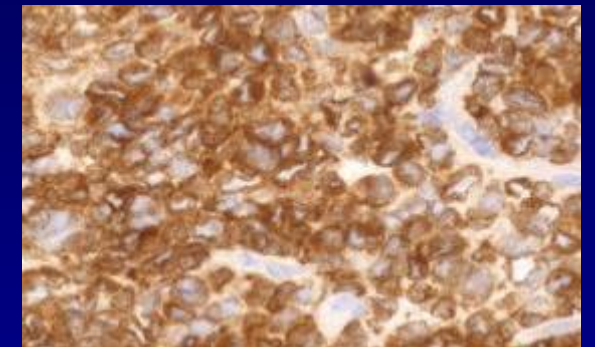
**AITL (3/6)**



**PTCL-NOS (7/11)**



**ALCL (6/8)**



- AITL: Angio-Immuno-blastic T-cell Lymphoma;
- PTCL: Peripheral T-Cell Lymphoma;
- ALCL: Anaplastic Large cell Lymphoma.

**Pierluigi Porcu, MD**

# Lacutamab: Phase I data

# Phase 1 Trial Design and Key Results in SS patients

*FDA Fast Track Designation granted based on these results*

## Total 44 patients with CTCL ≥ 2 lines of therapy

- 25 (incl. 20 SS) in dose escalation (intra-patient dose escalation was allowed)
- 19 (incl. 15 SS) in cohort expansion

**Recommended Phase 2 Dose:** 750mg QW x 4 then Q2W x 10 then Q4W until progression

## Safety:

- Maximum tolerated dose was not reached
- No DLT<sup>1</sup>s. Most common AE<sup>2</sup>: lymphopenia, fatigue (mostly grade 1–2)

## Mavoric<sup>3</sup> Phase 3 efficacy results for SS ≥ 1 line (without LCT<sup>4</sup>):

- Mogamulizumab: ORR: 37% | TTNT<sup>5</sup>: 12.9 months
- Comparator: Vorinostat<sup>6</sup>: ORR: 2% | TTNT: 3.3 months

<sup>1</sup>DLT = dose limiting toxicity

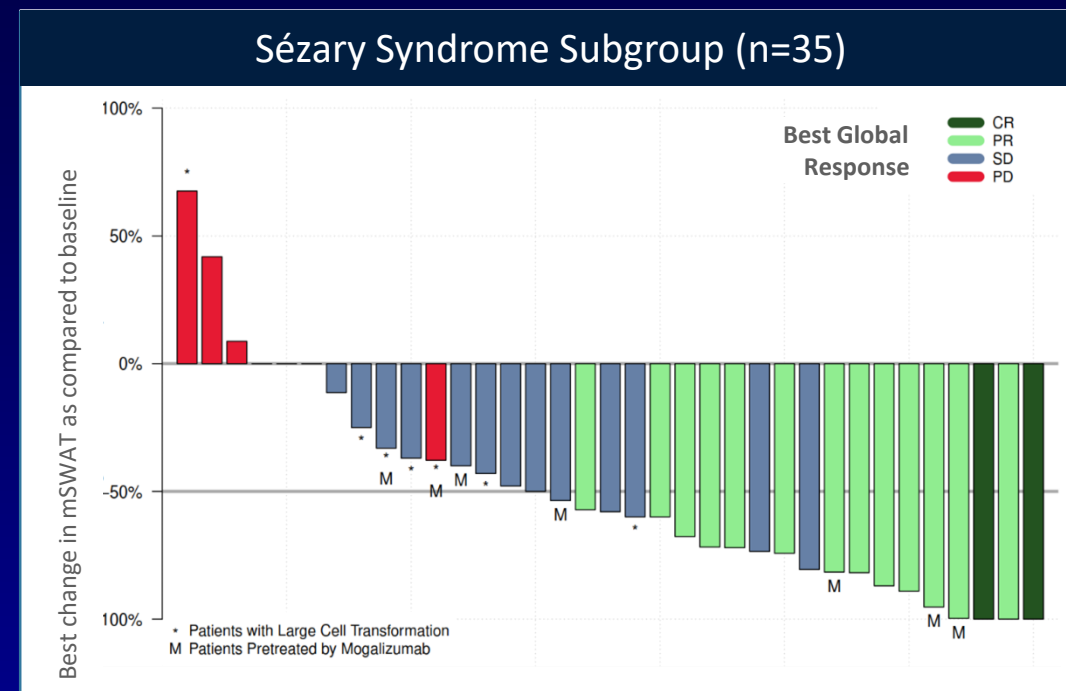
<sup>2</sup>AE = adverse event

<sup>3</sup>MAVORIC trial: Mogamulizumab vs. vorinostat in previously-treated CTCL. Source: Kim et al, Lancet Oncology 2018

<sup>4</sup>LCT = large cell transformation

<sup>5</sup>TTNT = Time-to-Next Significant Treatment

<sup>6</sup>Only drug approved in 2L+



|                      | All SS<br>N=35 | SS<br>without LCT <sup>2</sup><br>N=28 | Prior<br>mogamulizumab<br>N=7 |
|----------------------|----------------|----------------------------------------|-------------------------------|
| Best global response | 42.9%          | 53.6%                                  | 42.9%                         |
| DOR                  | 13.8           | 13.8                                   | 13.8                          |
| PFS                  | 11.7           | 12.8                                   | 16.8                          |

**Pierluigi Porcu, MD**

# Representative PATIENT pictures: PATIENT 11-024

Patient 11-024:

- 75-year old male
- Sézary Syndrome diagnosed in AUG 2011
- 6 lines of previous therapies (incl. MTX, INF $\alpha$ , vorinostat then mogamulizumab, BEX, pembrolizumab)
- Started at 3 mg/kg on 16OCT16
- Global PR since W14 (3 mg/kg)

*As of June 2017*

Screening



W28 Sustained PR



**Pierluigi Porcu, MD**

# Putting Lacutamab Phase 1 Data into Clinical Context

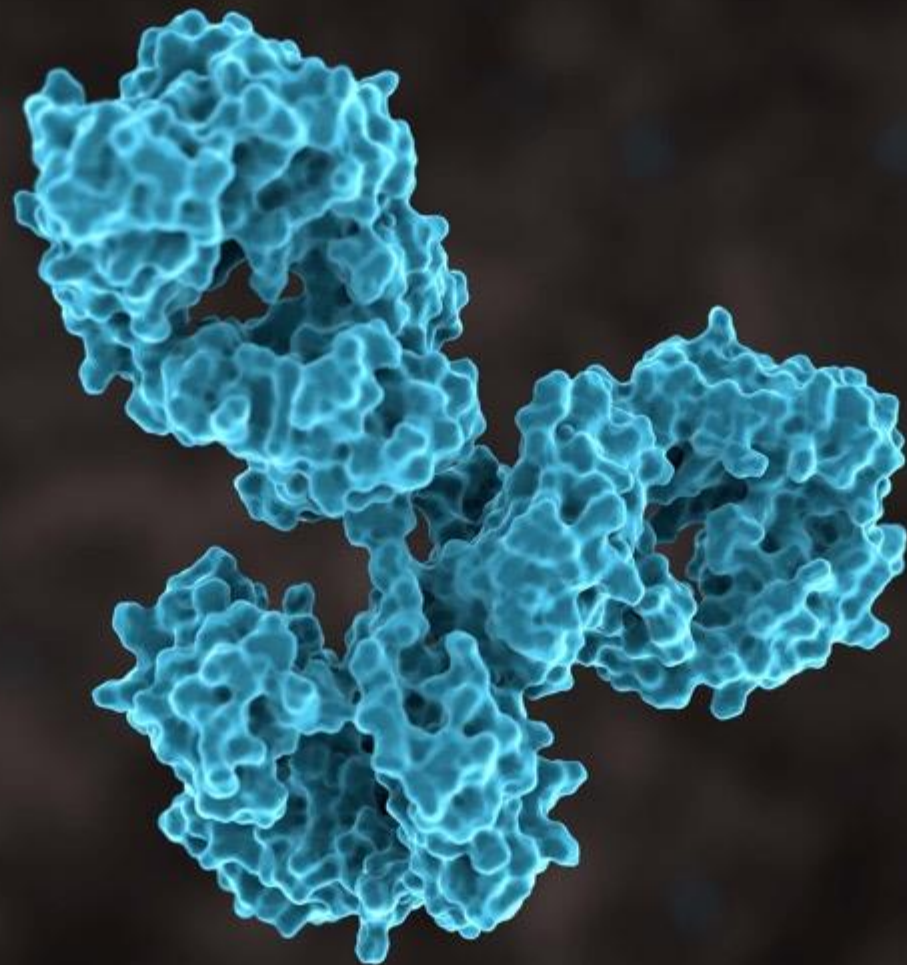
## Recent results in MF/SS patients

|                                  | Mogamulizumab                                                    | Vorinostat                                                         |
|----------------------------------|------------------------------------------------------------------|--------------------------------------------------------------------|
| Patient population               | Patients who received at least <u>one</u> prior systemic therapy |                                                                    |
| Response rate                    | MF/SS: 28%<br>MF: 21%<br>SS: 37%                                 | MF/SS: 5%<br>MF: 7%<br>Sézary: 2%                                  |
| Median progression-free survival | MF/Sézary: 7.7 months                                            | MF/Sézary: 3.1 months                                              |
| Time to next treatment*          | MF/SS: 11 months<br>MF: 8.8 months<br>SS: 12.9 months            | MF/SS: 3.5 months<br>MF: 4.1 months<br>Sézary: 3.3 months          |
| FDA label                        | Patients who received at least <u>one</u> prior systemic therapy | Patients who received at least <u>two</u> prior systemic therapies |

**Pierluigi Porcu, MD**

# Main Conclusions

- SS represents an area of highest unmet medical need within CTCL
  - Lacutamab has promising activity with 43% Global Response highly meaningful. If data confirmed in TELLOMAK > important paradigm shift in SS patients with  $\geq 2$  prior systemic therapies
- MF most common CTCL subtype; patients often suffer poor QoL secondary to skin infiltration by tumor cells.
  - Activation of stage 2 of TELLOMAK cohort 2 (KIR3DL2 expressing) shows proof of concept preliminary activity with Lacutamab in these patients. More mature data needed to measure actual magnitude of benefit
- Limited advances have been observed in the field of PTCL with exception of CD30 targeting, mostly in ALCL.
  - There is a high need for novel agents that can improve outcomes, particularly in R/R setting
  - Available scientific rationale supports the investigation of Lacutamab in PTCL, as monotherapy and in combination.



# Olivier Hermine, MD, PhD

*Professor of Hematology at the University of Paris Descartes*

*Director, Division of Adult Hematology at Hôpital Universitaire Necker Enfants Malades*

*Head of Lab. Cell. and mol. mechanisms of hematological disorders and therapeutic implications, INSERM U1163/Imagine Institute*

*Member of the Académie des Sciences & Principal Investigator of the LYSA Phase 2 KILT, France*





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# Introducing LYSA & LYSARC

TOMORROW, BETTER TREATMENT FOR  
LYMPHOMA PATIENTS

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# Our Network

- Cooperative network of **+500 lymphoma specialists**
- **120+ centers**
- **4 countries:** France, Belgium, Portugal, Israel
- Numerous **international collaborations**
- Strong track record for oncology **breakthroughs**



+ Instituto Português de Oncologia of Lisbon  
+ Sheba Medical Center of Tel Aviv



# Our Missions



Disseminate knowledge on lymphoma

→ scientific journals, international congresses, towards patients

**130+**  
**Research Projects**



Gather lymphoma specialists

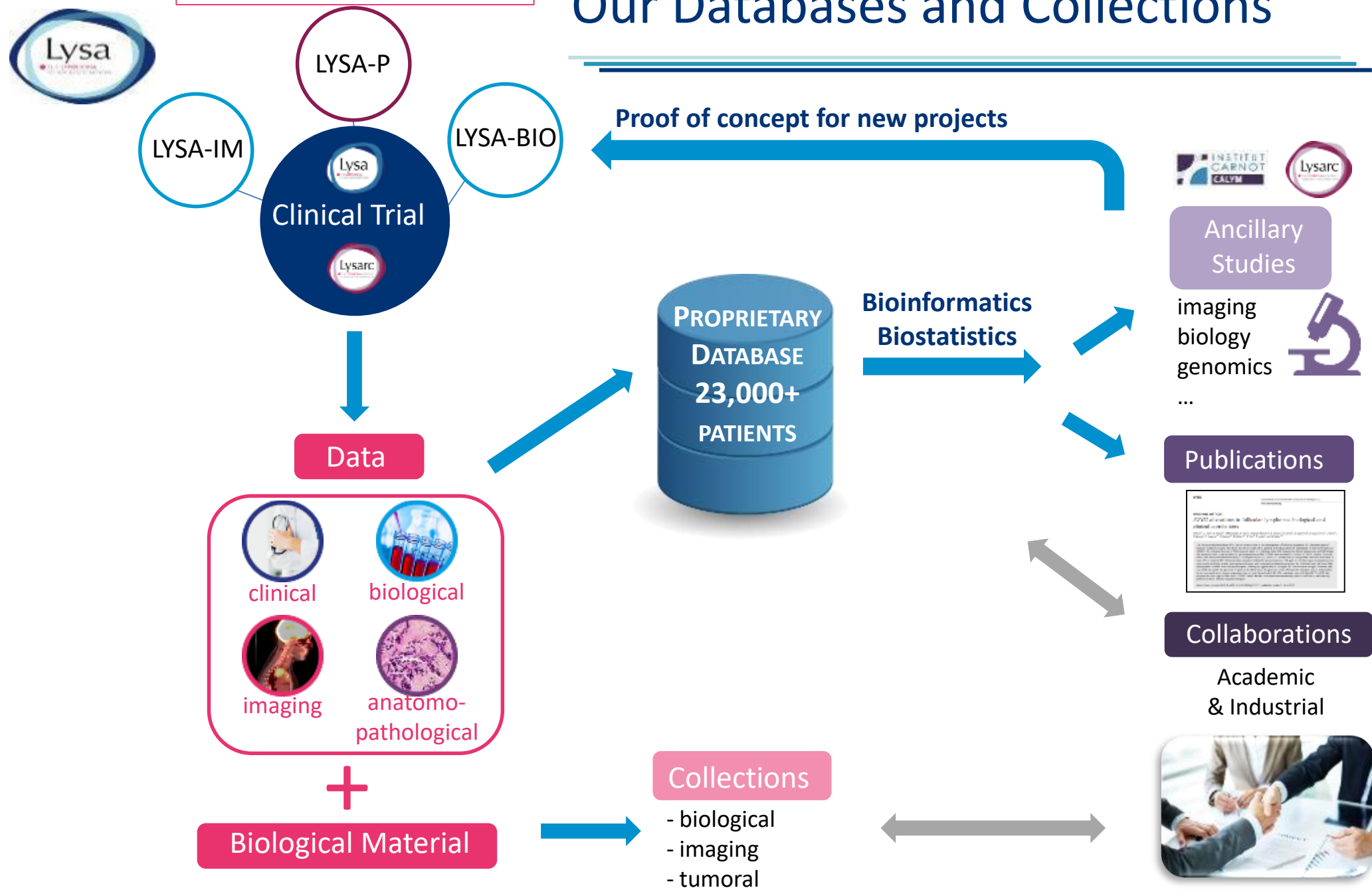
→ organized network of professionals and opinion leaders



Design research programs and clinical trial protocols

→ at all stages of the disease  
→ from phase 1 to 4, long-term follow-up  
→ clinical, biological, anatomo-pathological and epidemiological studies

**30,000+ studied patients**





# A Visible Contribution to the Progress of Adult Lymphoma Therapy

- Landmark **phase II & III trials**
  - benefit of rituximab in diffuse large cell lymphoma and in follicular lymphoma (former GELA group)
  - role of adjuvant radiotherapy in localized lymphoma, first studies with PET-CT adapted therapy
- Identification and characterization of **key biomarkers**
  - host genomics, plasma derived biomarkers, gene expression by RT-MLPA, immunomonitoring of blood subpopulations, imaging
- High **scientific production**
  - +250 publications, presentations at main international congresses, scientific meeting organization
- Contributions at the **international level**
  - standards of lymphoma care, prognostic indices (IPI, FLIPI-1 and -2, ...), response criteria, surrogate endpoints (SEAL, FLASH, EFS-24),
  - standardization of PET-CT use in lymphoma staging and response assessment
  - WHO lymphoma classification updates





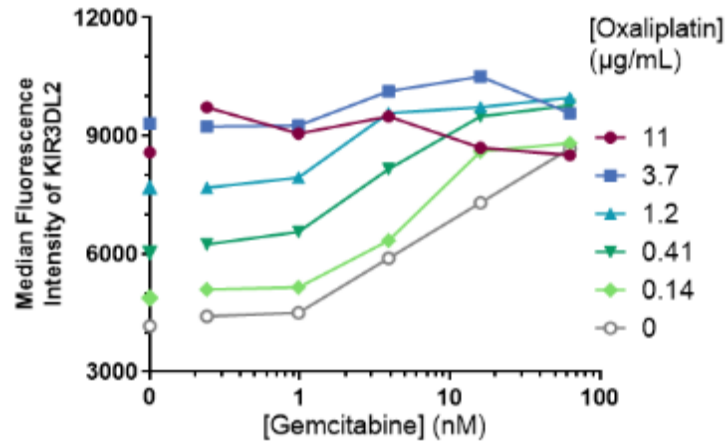
# LYSARC

The Lymphoma Academic Research  
Organisation

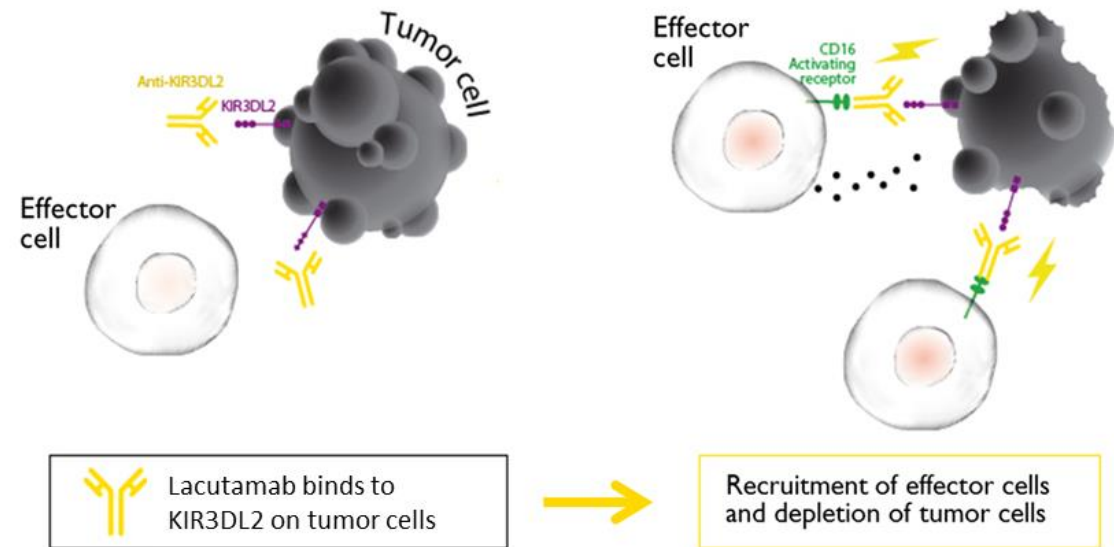
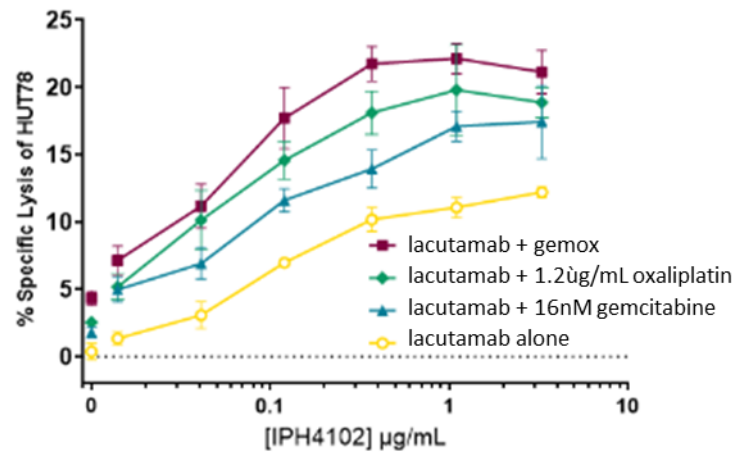
Rational for combining lacutamab with GEMOX

# Combination of Lacutamab with Gemox has synergistic anti-tumor activity *in-vitro*

Increased surface KIR3DL2 expression by GEMOX

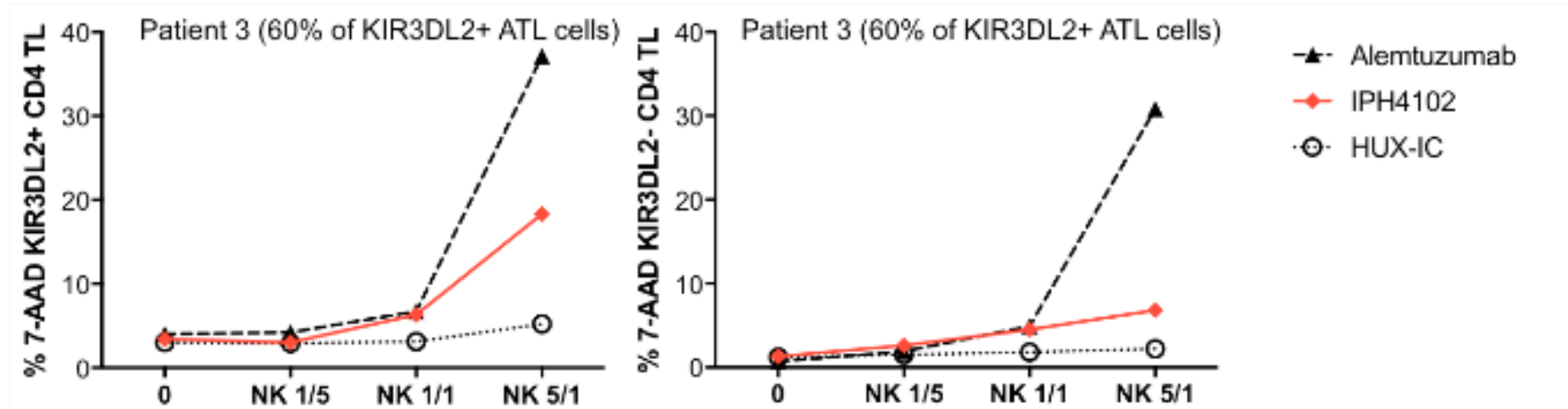


Enhanced ADCC of IPH4102 by GEMOX



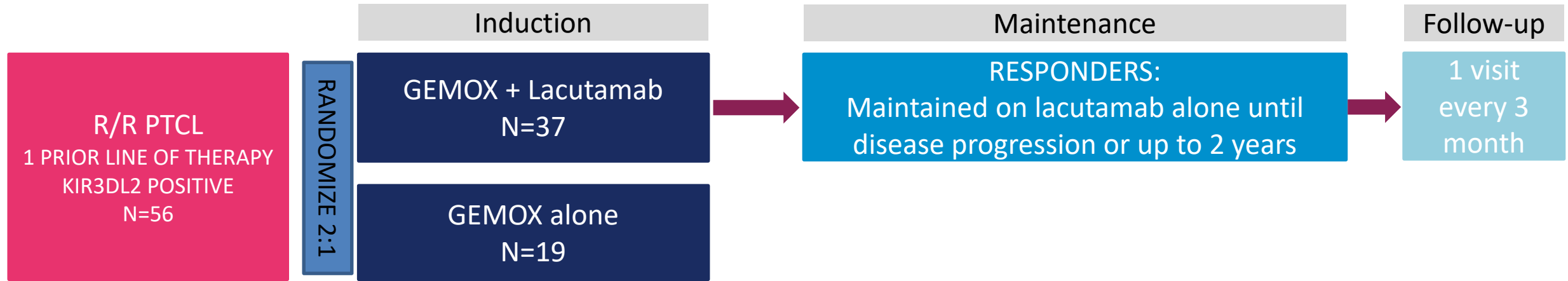
# Combination of Lacutamab with Gemox has synergistic anti-tumor activity *in-vitro*

Lacutamab efficiently eliminates KIR3DL2+ primary ATL tumor cells by autologous NK cells *ex vivo*





# KILT: Randomized Phase 2 Clinical Trial of Lacutamab in Combination with GEMOX in r/r PTCL



- **Primary endpoint:** median progression free survival
- **Key secondary endpoints:** response rate, toxicity and rate of overall survival at 12 months

**LYSA expects to initiate KILT study in 2H 2021**



# Global lacutamab overview

Joyson Karakunnel, MD, CMO



# Developing a New Standard of Care Across KIR3DL2-Expressing T-Cell Lymphomas

## Cutaneous T-Cell Lymphoma (CTCL)

## Peripheral T-Cell Lymphoma (PTCL)

### Phase 2 TELLOMAK Trial

#### Sezary Syndrome

**80-200 patients**

>90% KIR3DL2 expression

- Fast to market approach
- Niche indication with high unmet need
- Trial expanded (pivotal potential)
- Fast Track Designation & PRIME

#### Mycosis Fungoides

**2,200-4,400 patients**

~50% KIR3DL2 expression

- Expand potential beyond SS
- Explore impact of KIR3DL2 expression on clinical outcome
- Reached the pre-determined no. of responses needed to advance to stage 2
- Non expressors enrolling

#### Multi-trial Strategy From Relapsed to Frontline PTCL

**~18,000 patients**

~50% KIR3DL2 expression

- Monotherapy
- Combination + GemOX (LYSA) & SOC in relapsed setting
- Follow data into earlier lines (in combination with CHOP)



# Summary & Upcoming Catalysts

Mondher Mahjoubi, MD, CEO



# Summary: Driving Value Across our Business



## Driving near-term value with Lacutamab

- Deliver TELLOMAK with read-outs beginning in 2021
- Start of PTCL program



## Progressing an innovative and robust R&D portfolio

- Advancing NK cell-targeted portfolio
- Monalizumab – ongoing Phase 3 trial in H&N cancers



## Building a sustainable business

- Strengthen financial position
- Cash horizon to end 2022

Harnessing innate immunity to create novel therapeutics in areas of unmet medical need

# Key Catalysts Over the Next 24 Months

2 0 2 1

## LACUTAMAB

- Preliminary Phase 2 efficacy data in MF
- Start of PTCL studies

## MONALIZUMAB

- Preliminary data on the combination of monalizumab, cetuximab and durvalumab in IO-naïve patients with R/M SCCHN

## PRECLINICAL

- Update on NKCE platform development

2 0 2 2

## LACUTAMAB

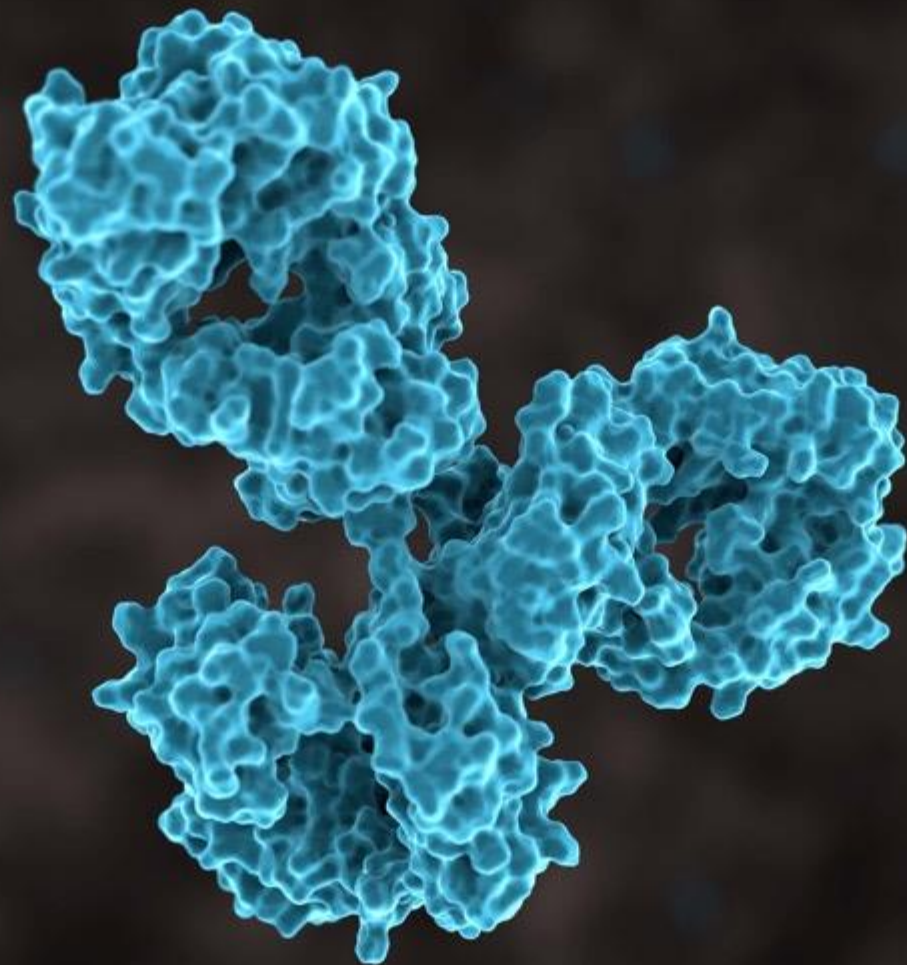
- Preliminary Phase 2 efficacy data in SS
- Stage 2 MF data

## AVDORALIMAB

- BP Phase 2 data

## PRECLINICAL

- Further progress with preclinical pipeline



Q&A



THANK YOU

[www.innate-pharma.com](http://www.innate-pharma.com)

PARIS: IPH.PA

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