Understanding the Potential of Lacutamab Across T Cell Lymphoma

February 9, 2021
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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
Innate’s Approach: Harnessing Innate Immunity in Cancer

Choosing the right targets to leverage the body’s immune response

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

2. Unleash NK cells
   - Monalizumab (NKG2A)

3. Reverse suppression
   - IPH5201 (CD39)
   - IPH5301 (CD73)

Adapted from Demaria et al., Nature 2019
# Innate’s Robust Pipeline Leveraging Expertise in Antibody Engineering & Innate Immunity Against Novel Cancer Targets

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

*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

<table>
<thead>
<tr>
<th>KIR3DL2 EXPRESSION</th>
<th>INCIDENCE Major markets (US, EU5, Japan), 2025</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>SEZARY SYNDROME</strong></td>
<td></td>
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<tr>
<td>• &gt;90% of patients express target*</td>
<td>~80–200 patients¹</td>
</tr>
<tr>
<td>• All tissues involved (skin, blood and lymph nodes)</td>
<td></td>
</tr>
<tr>
<td><strong>MYCOSIS FUNGOIDES</strong></td>
<td>2,200–4,000 patients¹</td>
</tr>
<tr>
<td>• ~50% of patients express target*</td>
<td></td>
</tr>
<tr>
<td><strong>PERIPHERAL T-CELL LYMPHOMA</strong></td>
<td>~18,000 patients²</td>
</tr>
<tr>
<td>• KIR3DL2 is expressed in multiple PTCL subtypes</td>
<td></td>
</tr>
<tr>
<td>• ~50% of patients express target*</td>
<td></td>
</tr>
</tbody>
</table>

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

2. PTCL: Delve Insights MR Report

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Phase 2 TELLOMAK Study Evaluating Lacutamab Across Subtypes of CTCL

Cohort #1 SS

SS all comers
(≥ 2 lines including mogamulizumab)
N=~60

Stage 1

Cohort #2 MF

MF KIR3DL2 Expressing
(≥ 2 prior systemic therapies)
N=21

→

Stage 2

Cohort #3 MF

MF KIR3DL2 non-Expressing
(≥ 2 prior systemic therapies)
N=18

MF KIR3DL2 Expressing
(≥ 2 prior systemic therapies)
N=29

MF KIR3DL2 non-Expressing
(≥ 2 prior systemic therapies)
N=20

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.
Data-Driven Strategy in PTCL

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

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

Figure 1 Source: Cancer Facts & Figures, 2019. American Cancer Society; 2019

- **Leukemia**: 35% (61,780 cases)
- **Myeloma**: 18% (32,110 cases)
- **Cutaneous T-cell lymphomas**: ~2,000-2,500/year
- **T-cell lymphomas**: ~10-12% (~8,500-9,500/year)
- **Non-Hodgkin’s Lymphomas**: ~20-30%
- **B-cell Lymphomas**: ~80% (~60,000/year)
- **Hodgkin's Lymphoma**: ~10% (~8500/year)

Total cases: 176,200
WHO 2016 Classification of T-Cell Neoplasms

- B-cell Neoplasms
- Non-Hodgkin’s Lymphomas (NHL)
- T/NK Cell Neoplasms

Mature T/NK Cell Neoplasms
- Cutaneous
  - Mycosis Fungoides
  - Sezary Syndrome
  - Primary Cutaneous CD30+ LPD
  - Primary Cutaneous Gamma/Delta TCL
  - HMB, Hydroa Vaccin Like Lymphoma
- Extranodal
  - Extramedullary NK/T Nasal Type (ENKTL)
  - Enteropathy-assoc. TCL (EATL)
  - Mon. Epithel Intest TCL (MEITL)
  - Hepatosplenic TCL (HSTCL)
  - Subcutaneous Panniculitis TCL
- Nodal
  - Peripheral T-cell Lymphoma (PTCL)-NOS
  - Anaplastic Large Cell Lymphoma ALK-Pos
  - Anaplastic Large Cell Lymphoma ALK-Neg
  - Angioimmunoblastic TCL (AITL)
- Leukemic
  - Adult T-cell Leukemia/Lymphoma (AITL)
  - Aggressive NK-Cell Leukemia (ANKL)
  - T-cell Prolymphocytic Leukemia (TPLL)
  - T-cell Large Granular Lymph. (LGL) Leukemia
- Provisional
  - Indolent T-cell LPD of the GI tract
  - Breast Implant Assoc. ALCL
  - Primary Cutaneous Acral CD8+ T-cell lymphoma
  - Primary Cutaneous CD8+ Aggress Epiderm. Cytotoxic TCL
  - Primary Cutaneous CD4 Small/Medium T-cell LPD

Precursor T/NK Cell Neoplasms

- T-cell ALL/LBL

Epstein Barr Virus
HTLV-1
Not Aggressive
Aggressive
Multiple Subtypes

Pierluigi Porcu, MD
Cutaneous T-cell Lymphomas
CTCL Incidence Varies by Subtype, Subtypes Difficult to Diagnose

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

### CTCL Subtype (WHO-EORTC Classification 2018)\(^2\)

<table>
<thead>
<tr>
<th>Subtype Split: Most likely [Range]</th>
<th>Geo.</th>
<th>% SS</th>
<th>% MF</th>
<th>% Oth. CTCL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Most likely</td>
<td>US(^1)</td>
<td>1% [1%-2%]</td>
<td>56% [53%-59%]</td>
<td>43% [39%-46%]</td>
</tr>
<tr>
<td>5EU(^2)</td>
<td>4% [3%-6%]</td>
<td>62% [57%-68%]</td>
<td>34% [26%-40%]</td>
<td></td>
</tr>
<tr>
<td>JP(^3)</td>
<td>1.5% [1%-2%]</td>
<td>63% [45%-65%]</td>
<td>35.5% [33%-54%]</td>
<td></td>
</tr>
</tbody>
</table>

### 5-Year Survival

<table>
<thead>
<tr>
<th>CTCL Subtype</th>
<th>5-Year Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mycosis fungoides (MF)</td>
<td>88%</td>
</tr>
<tr>
<td>Mycosis fungoides variants Folliculotropic MF Pagetoid reticulosis Granulomatous slack skin</td>
<td>75% 100% 100%</td>
</tr>
<tr>
<td>Sézary syndrome (SS)</td>
<td>36%</td>
</tr>
<tr>
<td>Primary cutaneous CD30+ LPDs C-ALCL LyP</td>
<td>95% 99%</td>
</tr>
<tr>
<td>Subcutaneous panniculitis-like TCL</td>
<td>87%</td>
</tr>
<tr>
<td>Primary cutaneous g/d T-cell lymphoma</td>
<td>11%</td>
</tr>
<tr>
<td>Primary cutaneous PTCL, NOS</td>
<td>15%</td>
</tr>
</tbody>
</table>

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1 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]
2 Meta-analysis ranges specific to region is used -- Dobos, G. et al. (2020)
3 Based on Meta-Analysis covering Asian Population (2,187 CTCL Patients) and most recent Japanese Study -- Dobos, G. et al. (2020); K. Fuji et al. (2020) [Data for 2012-2017, N=2090 CTCL, CBCL]; Hamada, T., et al. (2014)

* 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; *Data from: Cutaneous Lymphoma Foundation
Mycosis Fungoides: A low grade CD4+ T-cell lymphoma

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
What is Sezary Syndrome?

Three clinical elements to determine response in SS
1. Erythroderma (Skin)
2. Circulating Tumor Cells (Blood)
3. Lymphadenopathy (Lymph Nodes)

Overlap with MF

Stage N3
Blood
Stage B_2

Psoriasis
Eosinophilia
Increased IgE
Th2

Mycosis Fungoides

Erythroderma
Stage T4

Idiopathic

PRP
Drug Reactions

Atopic Dermatitis

Benign Dermatoses

Key lineage markers
CTLA-4, CD28, PD-1 Immune Checkpoints
CD45RO Memory T cell
KIR3DL2 CD158k
CLA^+ CCR4^+ Skin homing ^

Sezary Cell
Biomarkers

FoxP3?
GATA3
IL-15
IL-12, IFNγ, STAT4
Th2 Skewing

CD7
Lost

Pierluigi Porcu, MD

Lymph Nodes
Stage N3
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

Agar et al. JCO 2010;28:4730-4739
Quaglino et al. Cancer 2012
Kim Y et al, Arch Dermatol 1999
Natural Course of MF – Indolent but progressive, lifelong poor QoL, multiple sequential therapies, not curable

Mycosis Fungoides
median survival for all comers ~15 years

Sezary Syndrome
median survival 2-3 years

Quality of Life

Time (2-5 years)
Skin Directed Therapy

Time (5-8 years)
Systemic Therapy 1, 2, 3, 4, 5, 6

Time (2-3 years)
Sequencing of Multiple Systemic Therapies

Pierluigi Porcu, MD
### Six Systemic Agents are Approved for CTCL Treatment

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

Systemic Treatment Options in CTCL

<table>
<thead>
<tr>
<th>Line</th>
<th>Mycosis fungoides</th>
<th>Sézary syndrome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st</td>
<td>Bexarotene, bexarotene-based combinations</td>
<td>ECP, Bexarotene + interferon</td>
</tr>
<tr>
<td>2nd</td>
<td>Brentuximab / Mogamulizumab</td>
<td>Mogamulizumab</td>
</tr>
<tr>
<td>3rd</td>
<td>Romidepsin / vorinostat ^</td>
<td></td>
</tr>
<tr>
<td>4th</td>
<td>Interferon, methotrexate, gemcitabine, liposomal-doxorubicin</td>
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</tr>
</tbody>
</table>

^ only available in the US
Peripheral T-cell Lymphomas
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, 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).

Progression Free Survival (PFS): Relapsed/Refractory PTCL

BCCA N=153
3.7 months

Romidepsin N=130
4 months

Brentuximab N=56 (ALCL)
13.3 months

Pralatrexate N=109
3.5 months

Belinostat N=129
1.6 months

Brentuximab
- PTCL N=21
-AITL N=13

6.7 months

1.6 months

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”

<table>
<thead>
<tr>
<th></th>
<th>1st line</th>
<th>2nd line</th>
<th>≥ 3rd line</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CD30 expressing</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>~40% (mostly ALCL)</td>
<td>Brentuximab CHP</td>
<td></td>
<td>Combination chemotherapy (e.g. GemOx, DHAP)</td>
</tr>
<tr>
<td><strong>CD30 non-expressing</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>~60%</td>
<td>CHOP-like chemo</td>
<td></td>
<td>Romidepsin (FDA approved) Pralatrexate (FDA approved) Belinostat (FDA approved) Single agent chemo (Gemcitabine)</td>
</tr>
</tbody>
</table>

### ORR

- **CD30+**
  - ~80%
  - ~70%

- **CD30-**
  - ~45%
  - ~45%

### PFS

- **CD30+**
  - ~48mo
  - ~20mo

- **CD30-**
  - ~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
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: Angio-Immunoblastic T-cell Lymphoma;
- PTCL: Peripheral T-Cell Lymphoma;
- ALCL: Anaplastic Large cell Lymphoma.

M. Cheminant et al, ICML 2019
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 DLTs. Most common AE: lymphopenia, fatigue (mostly grade 1–2)

**Mavoric Phase 3 efficacy results for SS ≥ 1 line (without LCT):**
- Mogamulizumab: ORR: 37% | TTNT: 12.9 months
- Comparator: Vorinostat: ORR: 2% | TTNT: 3.3 months

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<table>
<thead>
<tr>
<th></th>
<th>All SS N=35</th>
<th>SS without LCT N=28</th>
<th>Prior mogamulizumab N=7</th>
</tr>
</thead>
<tbody>
<tr>
<td>Best global response</td>
<td>42.9%</td>
<td>53.6%</td>
<td>42.9%</td>
</tr>
<tr>
<td>DOR</td>
<td>13.8</td>
<td>13.8</td>
<td>13.8</td>
</tr>
<tr>
<td>PFS</td>
<td>11.7</td>
<td>12.8</td>
<td>16.8</td>
</tr>
</tbody>
</table>

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1. DLT = dose limiting toxicity
2. AE = adverse event
3. MAVORIC trial: Mogamulizumab vs. vorinostat in previously-treated CTCL. Source: Kim et al, Lancet Oncology 2018
4. LCT = large cell transformation
5. TTNT = Time-to-Next Significant Treatment
6. Only drug approved in 2L+
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, INFα, vorinostat then mogamulizumab, BEX, pembrolizumab)
- Started at 3 mg/kg on 16OCT16
- Global PR since W14 (3 mg/kg)

As of June 2017
Putting Lacutamab Phase 1 Data into Clinical Context

Recent results in MF/SS patients

<table>
<thead>
<tr>
<th></th>
<th>Mogamulizumab</th>
<th>Vorinostat</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Patient population</strong></td>
<td>Patients who received at least one prior systemic therapy</td>
<td></td>
</tr>
<tr>
<td><strong>Response rate</strong></td>
<td>MF/SS: 28% MF: 21% SS: 37%</td>
<td>MF/SS: 5% MF: 7% Sézary: 2%</td>
</tr>
<tr>
<td><strong>Median progression-free survival</strong></td>
<td>MF/Sézary: 7.7 months</td>
<td>MF/Sézary: 3.1 months</td>
</tr>
<tr>
<td><strong>Time to next treatment</strong>*</td>
<td>MF/SS: 11 months MF: 8.8 months SS: 12.9 months</td>
<td>MF/SS: 3.5 months MF: 4.1 months Sézary: 3.3 months</td>
</tr>
<tr>
<td><strong>FDA label</strong></td>
<td>Patients who received at least one prior systemic therapy</td>
<td>Patients who received at least two prior systemic therapies</td>
</tr>
</tbody>
</table>
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 >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
Introducing
LYSA & LYSARC

TOMORROW, BETTER TREATMENT FOR
LYMPHOMA PATIENTS
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

- Gather lymphoma specialists
  → organized network of professionnals 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

130+ Research Projects
Our Databases and Collections

Proprietary Database
23,000+ Patients

Proof of concept for new projects

Bioinformatics
Biostatistics

Ancillary Studies
Imaging, biology, genomics, ...

Publications

Collaborations
Academic & Industrial

Clinical Trial

LYSA-P
LYSA-IM
LYSA-BIO

Data

Biological Material

Clinical
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Imaging
Anatomo-pathological

+ 30,000+ studied patients

Collections
- biological
- imaging
- tumoral

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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
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

Cheminant M et al, ICML 2019
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)

- **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

Peripheral T-Cell Lymphoma (PTCL)

- **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

<table>
<thead>
<tr>
<th>Year</th>
<th>LACUTAMAB</th>
<th>MONALIZUMAB</th>
<th>PRECLINICAL</th>
</tr>
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</table>
| 2021 | • Preliminary Phase 2 efficacy data in MF  
      • Start of PTCL studies | • Preliminary data on the combination of monalizumab, cetuximab and durvalumab in IO-naïve patients with R/M SCCHN | • Update on NKCE platform development |
| 2022 | • Preliminary Phase 2 efficacy data in SS  
      • Stage 2 MF data | • BP Phase 2 data | • Further progress with preclinical pipeline |
THANK YOU

www.innate-pharma.com