LACUTAMAB IN PATIENTS WITH MYCOSIS FUNGOIDES (MF): EFFICACY RESULTS ACCORDING TO UPDATED LYMPH NODE (LN) CLASSIFICATION IN THE TELLOMAK STUDY

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Clinicaltrials.gov: NCT03902184
## Conflict of Interest Disclosure

<table>
<thead>
<tr>
<th>Conflict of Interest</th>
<th>Martine Bagot</th>
</tr>
</thead>
<tbody>
<tr>
<td>Relationships with companies that may be relevant to the meeting</td>
<td>• Innate Pharma, Helsinn/Recordati, Kyowa Kirin, Takeda</td>
</tr>
<tr>
<td>• Sponsorship of financial support for research</td>
<td>• None</td>
</tr>
<tr>
<td>• Fees or other (financial) compensation</td>
<td>• None</td>
</tr>
<tr>
<td>• Shareholder</td>
<td>• None</td>
</tr>
<tr>
<td>• Other relation, namely Scientific Boards</td>
<td>• Innate Pharma, Helsinn/Recordati, Kyowa Kirin, Takeda</td>
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</tbody>
</table>
Lacutamab

**KIR3DL2 targeted treatment in T-Cell Lymphoma – Phase 1 data**

- First-in-class humanized anti-KIR3DL2 cytotoxicity-inducing antibody under development for the treatment of T-cell lymphomas:
  - Cutaneous T-cell lymphoma (CTCL) including Sézary Syndrome (SS)\(^1\) & Mycosis Fungoides (MF)\(^2\)
  - Peripheral T-cell lymphoma (PTCL)

- Phase 1\(^1\) data in mainly SS patients who have been treated by at least two prior systemic therapies:
  - Global Objective Response Rate (ORR): 42.9% (95%CI: 28.0–59.1)
  - Median duration of response (DoR): 13.8 months (95%CI: 7.2–NA)
  - Median progression free survival (PFS): 11.7 months (95%CI: 8.1–NA)

- In recognition of high-unmet need and early potential, lacutamab has been granted key designations
  - Orphan drug designation for the treatment of CTCL (EMA and FDA)
  - PRIME (EMA) and Fast Track (FDA) designation for SS patients who have received at least 2 prior systemic therapies

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**Figure 1: Lacutamab Mechanism of Action**

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<table>
<thead>
<tr>
<th>INDICATION &amp; KIR3DL2 EXPRESSION</th>
<th>INCIDENCE (US, EU5, Japan),</th>
</tr>
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<tbody>
<tr>
<td><strong>SEZARY SYNDROME</strong></td>
<td></td>
</tr>
<tr>
<td>• &gt;90% of patients express target*</td>
<td>~80–200 patients(^1)</td>
</tr>
<tr>
<td>• All tissues involved</td>
<td></td>
</tr>
<tr>
<td>(skin, blood and lymph nodes)</td>
<td></td>
</tr>
<tr>
<td><strong>MYCOsis FUNGOIDES</strong></td>
<td></td>
</tr>
<tr>
<td>• ~50% of patients express target*</td>
<td>2,200–4,000 patients(^1)</td>
</tr>
</tbody>
</table>

2. Lugano 2021, EORTC 2021
**TELLOMAK**  
*Phase 2 Study in Two CTCL Subtypes (MF and SS) - NCT03902184*

**Administration**
- Lacutamab is administered by intravenous infusion every week for 5 weeks then every 2 weeks for 10 administrations then every 4 weeks, until disease progression or unacceptable toxicity

**Study Endpoints**
- Primary endpoint: global ORR
- Secondary endpoints: PFS, DoR, quality of life, safety and tolerability, PK & immunogenicity

**Key Eligibility Criteria**
- Relapsed and/or refractory stage IB-IV MF; ECOG performance status ≤2
- KIR3DL2 ≥ 1% (Cohort 2) or <1% (Cohort 3) based on central evaluation by immunohistochemistry (IHC)*
- No evidence of large cell transformation (LCT) based on central histologic evaluation at screening

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**Cohort #1**
- SS  
  - (≥ 2 prior systemic therapies)  
  - N ≈ 60

**Cohort #2**
- MF KIR3DL2 Expressing (≥ 1%)  
  - (≥ 2 prior systemic therapies)  
  - N=21

**Cohort #3**
- MF KIR3DL2 non Expressing (< 1%)  
  - (≥ 2 prior systemic therapies)  
  - N=18

**Cohort All comers**
- MF KIR3DL2 Expressing (≥ 1%) and non Expressing (< 1%)  
  - (≥ 2 prior systemic therapies)  
  - N up to 37

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**Stage 1 of a Simon 2-stage design**
- ≥ 3 responses

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**ORR**: Objective Response Rate; **DoR**: duration of response; **PFS**: progression free survival  
* KIR3DL2 expression by IHC assay for use on frozen tissue
• Global Response requires assessment of all compartments (Olsen 2011)

• LN response assessment challenging if:
  • LN clinically abnormal but not biopsy-proven (Nx)
  • LN is enlarged due to inflammation (N1, N2)

• According to updated Olsen 2022 criteria LN involvement with lymphoma requires N3 pathology classification
**TELLOMAK**

**LN Assessment by Updated Response Criteria (Olsen 2022)**

Clinical evaluation of LN

- **No Clinically abnormal LN**
  - <1.5 cm LDi confirmed by imaging
  - Biopsy not necessary
  - **N0**

- **Clinically abnormal LN**
  - >1.5 cm LDi confirmed by imaging
  - Biopsy necessary
  - Biopsy (Pathological determination) not done
    - **Nx**
  - Biopsy (Pathological determination) done
    - **N1**
    - **N2**
    - **N3**

Per Olsen 2011
All N categories are considered as involved

Per Olsen 2022
Only N3 categories is considered as involved

**Patient characteristics of MF cohorts 2 and 3**

<table>
<thead>
<tr>
<th></th>
<th>Cohort 2 MF KIR3DL2 ≥ 1%* (N= 21)</th>
<th>Cohort 3 MF KIR3DL2 &lt; 1%* (N=18)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age in years, Median (range)</td>
<td>59 (33-77)</td>
<td>58 (19-81)</td>
</tr>
<tr>
<td>• Female, N (%)</td>
<td>7 (33%)</td>
<td>3 (17%)</td>
</tr>
<tr>
<td>• Male, N (%)</td>
<td>14 (67%)</td>
<td>15 (83%)</td>
</tr>
<tr>
<td>• Stage IB / II, N (%)</td>
<td>16 (76%)</td>
<td>15 (83%)</td>
</tr>
<tr>
<td>• Stage III¹, N (%)</td>
<td>5 (24%)</td>
<td>3 (17%)</td>
</tr>
<tr>
<td>Blood involvement², N (%)</td>
<td>8 (38%)</td>
<td>4 (22%)</td>
</tr>
<tr>
<td>Nodal Stage at Baseline, N (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• N0</td>
<td>10 (47.6%)</td>
<td>9 (50%)</td>
</tr>
<tr>
<td>• N1</td>
<td>2 (9.5%)</td>
<td>3 (16.7%)</td>
</tr>
<tr>
<td>• N2</td>
<td>2 (9.5%)</td>
<td>1 (5.5%)</td>
</tr>
<tr>
<td>• N3</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>• Nx</td>
<td>7 (33.3%)</td>
<td>5 (27.8%)</td>
</tr>
<tr>
<td>Prior systemic therapies, Median N (range)</td>
<td>4 (2-8)</td>
<td>4.5 (2-15)</td>
</tr>
<tr>
<td>Follow-up (months), Median (range)</td>
<td>12.2 (3-25)</td>
<td>13.8 (1-24)</td>
</tr>
</tbody>
</table>

1. Stage IV, SS not included
2. Blood involvement at baseline: B1
* KIR3DL2 expression by IHC assay for use on frozen tissue
## Preliminary Efficacy Results in Cohort 2 MF (KIR3DL2 ≥ 1%)

**Best Skin Response**
- **N=21**

<table>
<thead>
<tr>
<th>CR</th>
<th>PR</th>
<th>SD</th>
<th>PD</th>
<th>NE</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 (9.5%)</td>
<td>10 (47.6%)</td>
<td>7 (33.3%)</td>
<td>2 (9.5%)</td>
<td>2 (9.5%)</td>
</tr>
</tbody>
</table>

**Best Blood Response**
- **N=8**

<table>
<thead>
<tr>
<th>CR</th>
<th>PR</th>
<th>SD</th>
<th>PD</th>
<th>NE</th>
</tr>
</thead>
<tbody>
<tr>
<td>5 (62.5%)</td>
<td>0 (0%)</td>
<td>3 (37.5%)</td>
<td>0 (0%)</td>
<td>-</td>
</tr>
</tbody>
</table>

**Best Global Response by LN assessment**

<table>
<thead>
<tr>
<th><strong>N=21</strong></th>
<th><strong>Considering all N categories</strong></th>
<th><strong>Considering only Nx and N3 categories</strong></th>
<th><strong>Considering only N3 categories</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ORR % [95%CI]</strong></td>
<td>57.1% [36.5-75.5]</td>
<td>62.5% [30.6-86.3]</td>
<td>28.6% [13.8-50.0]</td>
</tr>
</tbody>
</table>

Global Clinical Benefit Rate (CBR) 90.5% [95% CI 71.1-97.3]

TELLOMAK
Preliminary Efficacy Results in Cohort 2 MF (KIR3DL2 ≥ 1%)

Best Global Response by LN involvement

According to updated Olsen 2022 criteria LN involvement with lymphoma requires N3 pathology classification

All N categories

- ORR % [95%CI]
  - N1
  - N2
  - N3
  - 28.6% [13.8-50.0]

Only Nx and N3

- ORR % [95%CI]
  - Nx
  - N3
  - 38.1% [20.8-59.1]

Only N3

- ORR % [95%CI]
  - N3
  - 42.9% [24.5-63.5]

Data cut-off (DCO): 04MAR2022
Per Olsen 2011
Per Olsen 2022
TELLOMAK
Preliminary Efficacy Results in Cohort 2 MF (KIR3DL2 ≥ 1%)

Best Overall Response
Olsen 2011 (N1, N2, N3, Nx involvement)

- 6 patients achieved Global Response (GR)
- Median time to GR: 1 month (range: 1.0-3.0)
- Median DoR: 10.2 months (95% CI: 4.6-N.A)

Best Overall Response
Olsen 2022 (N3 involvement)

- 9 patients achieved Global Response (GR)
- Median time to GR: 1 month (range: 0.9-4.7)
- Median DoR: 7.4 months (95% CI: 3.7-N.A)

Data cut-off (DCO): 04MAR2022
## Preliminary Efficacy Results in Cohort 3 MF (KIR3DL2 < 1%)

### Cohort 3 MF

**KIR3DL2 < 1\%**

<table>
<thead>
<tr>
<th>Response</th>
<th>Skin Response</th>
<th>Blood Response</th>
<th>Global Response by LN assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N=18</td>
<td>N=4</td>
<td>Considering all N categories</td>
</tr>
<tr>
<td></td>
<td>(%)</td>
<td>(%)</td>
<td>Considering only Nx and N3 categories</td>
</tr>
<tr>
<td>CR</td>
<td>0 (0%)</td>
<td>1 (25%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>PR</td>
<td>3 (16.7%)</td>
<td>0 (0%)</td>
<td>2 (11.1%)</td>
</tr>
<tr>
<td>SD</td>
<td>13 (72.2%)</td>
<td>2 (50%)</td>
<td>14 (77.8%)</td>
</tr>
<tr>
<td>PD</td>
<td>1 (5.6%)</td>
<td>0 (0%)</td>
<td>1 (5.6%)</td>
</tr>
<tr>
<td>NE</td>
<td>1 (5.6%)</td>
<td>1 (25%)</td>
<td>1 (5.6%)</td>
</tr>
</tbody>
</table>

**Global Clinical Benefit Rate (CBR)**: 88.9\% [95\% CI 67.2-96.9]

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**Data cut-off (DCO): 04MAR2022**

**Per Olsen 2011**

**Per Olsen 2022**

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CR: complete response, PR: partial response, SD: stable disease, PD: progressive disease; N: number, CBR: Clinical Benefit Rate, ORR: Overall Response Rate
## Preliminary Safety Results in Cohorts 2&3 (N=39)

### Any treatment-emergent AEs (TEAEs)

<table>
<thead>
<tr>
<th>Event / as defined by the treating investigator</th>
<th>Total N=39 n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any treatment-emergent AEs (TEAEs)</td>
<td>36 (92.3)</td>
</tr>
<tr>
<td>Any Lacutamab-related TEAEs</td>
<td>23 (59.0)</td>
</tr>
</tbody>
</table>

### Most frequent Lacutamab-related TEAEs

- Asthenia: 5 (12.8)
- Arthralgia: 4 (10.3)
- Nausea: 3 (7.7)

### Any Serious TEAEs (SAEs)

- Any Serious Lacutamab-related TEAEs: 2 (5.1)
- Any Grade 3/4/5 Lacutamab-related TEAEs: 2 (5.1)
- Any Lacutamab-related Death: 1 (2.6)

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1. Event / as defined by the treating investigator
2. NCI Common Terminology Criteria for Adverse Events (CTCAE)
3. 24Nov2020 Interstitial lung disease, Gr3 probably related, 11Nov2020 discontinued study treatment. Mar2022 Interstitial lung disease, Gr5 probably related

Data cut-off (DCO): 04MAR2022
• 68-year-old female
• MF diagnosed in 2016
• 4 previous lines of therapy (methotrexate, bexarotene, interferon, methotrexate)
• T2N0M0B1 at baseline
• Response:
  • Skin: PR from W5, CR from W37
  • Blood: CR from W5
  • LN: Not involved (N0 at baseline)
  • Global: PR from W5, CR from W37 still ongoing (last evaluation February 28, 2023)
TELLOMAK is a Phase 2 study evaluating lacutamab monotherapy in CTCL. Cohort 2 and 3 enroll R/R MF patients with ≥ 2 prior systemic therapies who express KIR3DL2 at the ≥ 1% and <1% level.

Lymph Node assessment is an important component of staging and response assessment in CTCL. The recent update to the consensus guidelines (Olsen 2022) states that LN involvement requires pathology fulfilling N3 criteria. Based on updated LN criteria:

- In Cohort 2 (KIR3DL2 ≥1%, N=21)
  - Global ORR 42.9% (95% CI [24.5; 63.5]) (Only N3) and 28.6% (95% CI [13.8-50.0]) (N1,N2, Nx, N3)
  - Blood ORR 62.5% (95% CI: 30.6-86.3)
  - Skin ORR 57.1% (95% CI: 36.5-75.5)
  - Clinical Benefit Rate 90.5% [95% CI 71.1-97.3]

- in Cohort 3 (KIR3DL2 < 1%, N=18)
  - Findings remain consistent

In this preliminary analysis of cohort 2 and 3 (N=39), lacutamab has clinical activity with favorable safety.

Updated assessment of LN status results in a higher global response, highlighting the impact of the adoption of the 2022 criteria on clinical trial design and outcome.
Acknowledgments

Thank you to all our investigators, experts, site staff, and ultimately the patients and their families.

In total 53 active sites

- France (10)
- Germany (8)
- Spain (6)
- Italy (4)
- Belgium (3)
- Austria (2)
- Poland (3)

Sponsor: Innate Pharma
Back up
# TELLOMAK

## 7 Nx patients in Cohort 2

<table>
<thead>
<tr>
<th>ID</th>
<th>LN stage</th>
<th>LN nb</th>
<th>Localisation</th>
<th>Size</th>
<th>Best LN response</th>
<th>Best global response Olsen 2011</th>
<th>Best global response Olsen 2022</th>
</tr>
</thead>
<tbody>
<tr>
<td>001-M-016</td>
<td>NX</td>
<td>1</td>
<td>Left iliac</td>
<td>2.0x1.5</td>
<td>SD</td>
<td>SD</td>
<td>PR</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2</td>
<td>Right external iliac</td>
<td>1.6x1.3</td>
<td>SD</td>
<td>SD</td>
<td></td>
</tr>
<tr>
<td>001-M-059</td>
<td>NX</td>
<td>1</td>
<td>Axillary left</td>
<td>1.5x1.5</td>
<td>SD</td>
<td>SD</td>
<td>SD</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2</td>
<td>Inguinal Right</td>
<td>2.6x1.8</td>
<td>SD</td>
<td>SD</td>
<td></td>
</tr>
<tr>
<td>001-M122</td>
<td>NX</td>
<td>1</td>
<td>Inguinal Left</td>
<td>1.5x0.9</td>
<td>SD</td>
<td>SD</td>
<td>SD</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2</td>
<td>Axillary Right</td>
<td>2.1x0.8</td>
<td>SD</td>
<td>SD</td>
<td></td>
</tr>
<tr>
<td>020-M070</td>
<td>NX</td>
<td>1</td>
<td>Axillary Right</td>
<td>1.6x1.3</td>
<td>SD</td>
<td>SD</td>
<td>SD</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2</td>
<td>Axillary Left</td>
<td>1.6x1.2</td>
<td>SD</td>
<td>SD</td>
<td></td>
</tr>
<tr>
<td>052-M-051</td>
<td>NX</td>
<td>7</td>
<td>Inguinal, Axillary only short axis is available 1.7; 1.8; 1.0; 0.8; 0.9; 0.9; 0.8; 1.8; 1.0</td>
<td>SD</td>
<td>SD</td>
<td>SD</td>
<td></td>
</tr>
<tr>
<td>101-M-028</td>
<td>NX</td>
<td></td>
<td>Scans not available</td>
<td></td>
<td></td>
<td>PR</td>
<td>PR</td>
</tr>
<tr>
<td>110-M-088</td>
<td>NX</td>
<td>6</td>
<td>Cervical, Axillary 1.5x1.0; 1.9x1.2; 1.5x1.3; 1.8x1.5; 1.8x1.1; 1.7x1.3; 1.6x1.1</td>
<td>SD</td>
<td>SD</td>
<td>SD</td>
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</tr>
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</table>

Data cut-off (DCO): 04MAR2022
3 patients previously assessed as Global SD are now classified as PR

<table>
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<tr>
<th></th>
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<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>001-M-016</td>
<td>NX</td>
<td>2</td>
<td>Left iliac Right external iliac</td>
<td>2.0x1.5, 1.6x1.3</td>
<td>PR</td>
<td>NI</td>
<td>SD/NI</td>
<td>SD</td>
<td>PR</td>
</tr>
<tr>
<td>042-M-053</td>
<td>N1</td>
<td>3</td>
<td>Axillary Right Inguinal Right Inguinal Left</td>
<td>1.9x1.8, 2.3x1.7, 2.4x1.4</td>
<td>PR</td>
<td>NI</td>
<td>SD/NI</td>
<td>SD</td>
<td>PR</td>
</tr>
<tr>
<td>104-M-106</td>
<td>N1b</td>
<td>5</td>
<td>Axillary right Axillary left Iliac left Inguinal right Iliac right</td>
<td>1.6x0.9, 4.1x1.8, 3.9x1.4, 2.2x1.4, 3.3x1.3</td>
<td>PR</td>
<td>NI</td>
<td>SD/NI</td>
<td>SD</td>
<td>PR</td>
</tr>
</tbody>
</table>