Clinical/Regulatory Updates of Burosumab and The Current Pre-launch Activities in EU

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Topics to be Updated

- Clinical Status Update of Burosumab
- Regulatory Update toward Approval in US and EU
- Pre-launch Activities in EU
Clinical Status Update
Clinical Status Update of Burosumab

What we have achieved in our clinical program

**Pharmacological effect**
- Reducing phosphate wasting
- Increase in serum P levels
- Increase in 1,25D levels

Clinical benefits

Hurdles in clinical development
- Orphan disease – limited number of patients
- Limited data and understanding on the disease
- New target molecule, FGF23 and monoclonal antibody
- No established pathway for regulatory approval

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Comprehensive Assessment of Clinical Effects

Phosphate metabolism
- Phosphate
- TmP/GFR
- 1, 25 VD

Bone metabolism
- Bone Parameters; ALP, P1NP, CTx

Muscle function

Rickets improvement

QOL improvement
- Pain
- Physical function
- Stiffness
- Walking 6MWT

Osteomalacia improvement
- Blue: ped./adult
- Red: ped. only
- Green: adult only

Radiographic data; RSS, RGI-C
- Growth data

Bone biopsy data
- Fracture data
# Clinical studies for XLH

<table>
<thead>
<tr>
<th>Study</th>
<th>Age</th>
<th>Study Title</th>
<th>status</th>
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<tbody>
<tr>
<td><strong>Pediatric Studies</strong> as of October 16th</td>
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<td></td>
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<tr>
<td>UX023-CL201</td>
<td>5-12</td>
<td>Open-label, dose finding, Ph2, n=52</td>
<td>ongoing</td>
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<tr>
<td>UX023-CL205</td>
<td>1-4</td>
<td>Open-label, single arm, Ph2, n=13</td>
<td>ongoing</td>
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<tr>
<td>UX023-CL002</td>
<td>5-14</td>
<td>Retrospective radiographs from patients on conventional therapy, n=52</td>
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<tr>
<td>UX023-CL301</td>
<td>1-12</td>
<td>Open-label, comparative study with conventional therapy, Ph3, n=61</td>
<td>ongoing</td>
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<tr>
<td><strong>Adult Studies</strong> as of October 16th</td>
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<tr>
<td>KRN23-US-02</td>
<td>Adult</td>
<td>Blinded, placebo-controlled, single-dose Ph1, n=38</td>
<td>completed</td>
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<tr>
<td>INT-001/002</td>
<td>Adult</td>
<td>Open-label, repeated-dose, Ph1/2, INT-001(n=29), INT-002(n=23)</td>
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<tr>
<td>KRN23-001</td>
<td>Adult</td>
<td>Open-label, single-dose, Ph1, n=18 (in Japan and Korea)</td>
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<tr>
<td>UX023-CL203</td>
<td>Adult</td>
<td>Open-label, repeated-dose, Ph2 extension study, n=20</td>
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<tr>
<td>UX023-CL303</td>
<td>Adult</td>
<td>Blinded, placebo-controlled Ph3, n=134 (including Japan and Korea)</td>
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<tr>
<td>UX023-CL304</td>
<td>Adult</td>
<td>Open-label, single-arm Ph3 (bone biopsy) n=14</td>
<td>ongoing</td>
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Clinical Status Updates Summary

- We believe we have conducted a comprehensive clinical program to understand the disease and potential benefits and risks of Burosumab.
- We believe that Burosumab addresses the major clinical aspects and important unmet medical needs in XLH.
- We believe that the totality of the data support a positive benefit-risk of Burosumab.
Regulatory Update
We are currently pursuing a conditional approval of pediatric indication (from one year olds to adolescents) first in EU and will subsequently file adult indication after approval of pediatric indication.

We are prioritizing the timing of approval for pediatric indication. This was to avoid any potential delays in the review procedure due to the large amount of recent data from the adult XLH Phase 3 study.
Key Milestones in near future

- CHMP opinion on peds. indication expected around the end of 2017
- Target date to get approval is within 67 days after CHMP opinion
- Initiate commercialization in Germany shortly after approval
- Adult indication filing planned after a decision is first reached on peds.
US Regulatory Update (1)

Process overview

- Breakthrough Therapy Designation for pediatric XLH received June 2016
- BLA was submitted in August to pursue pediatric and adult indications.
- Filing Acceptance/Priority Review designation letter received Oct; PDUFA date confirmed for 17 Apr 2018

October 27th, 2017
US Regulatory Update (2)

- Burosumab for the treatment of XLH designated as a drug for a “rare pediatric disease” and eligible for a Priority Review Voucher

- BLA filed for adults and peds. in August 2017 and includes:
  - 64 week Phase 2 data in 5-12 yr olds and 24 week Phase 2 data in 1-4 yr olds
  - Ongoing pediatric Phase 3 study not required
  - 24-week placebo-controlled Adult Phase 3 data including fracture healing data
  - Bone biopsy data from first two adult patients in the Phase 3 bone quality study. Data from additional patients to be submitted as supporting evidence when available during BLA review
Pre-launch Activities in EU
Major Pre-launch Activities in EU

- Commercial organization: Rare Disease Business Unit in KKI
- Disease awareness
- Patient and physician identification
- Branding and Marketing message preparation (not to be used pre-approval)
- Market Access (pricing)
- Supporting an XHL patient community in EU
- XLH Registry and Early access program (EAP)
Disease Awareness Activities

Disease awareness

Physicians
- Visits by MSL
- Conference/symposium
- XLH disease status slide

Patients
- Publication
- XLH link
- Patient organization
Disease Awareness Activities

xlhlink.com (for patients)
Launch date 21st Aug 17

About XLH
Managing XLH
Health & Wellness
Sharing Stories

xlhlinkhcp.com (for healthcare professionals)
Launch date end of 2017

About XLH
Manifestations
Diagnosis
Assessment
Resources
Patient Identification

- MSLs
- Clinical development program
- ISTs – database analyses and publication
- Conferences and KOL discussions
- Online burden of illness and patient surveys
Registry and EAP

- **Registry program**
  - Establish historical database to establish the burden of disease: retrospective analysis of patients with XLH and their clinical history
  - After approval, registry will include patients treated & untreated with Burosumab
    - This will allow comparison with concurrent and historical controls
    - Submitted to EMA to satisfy requirement for a post approval safety study (PASS)

- **EAP**
  - Plan to provide Burosumab treatment options in EU5 countries under the specified protocol before Burosumab becomes commercially available
  - EAP is only available for pediatric population and has initiated in Germany and Spain