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

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Topics to be Updated

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- 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

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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

Comprehensive Assessment of Clinical Effects

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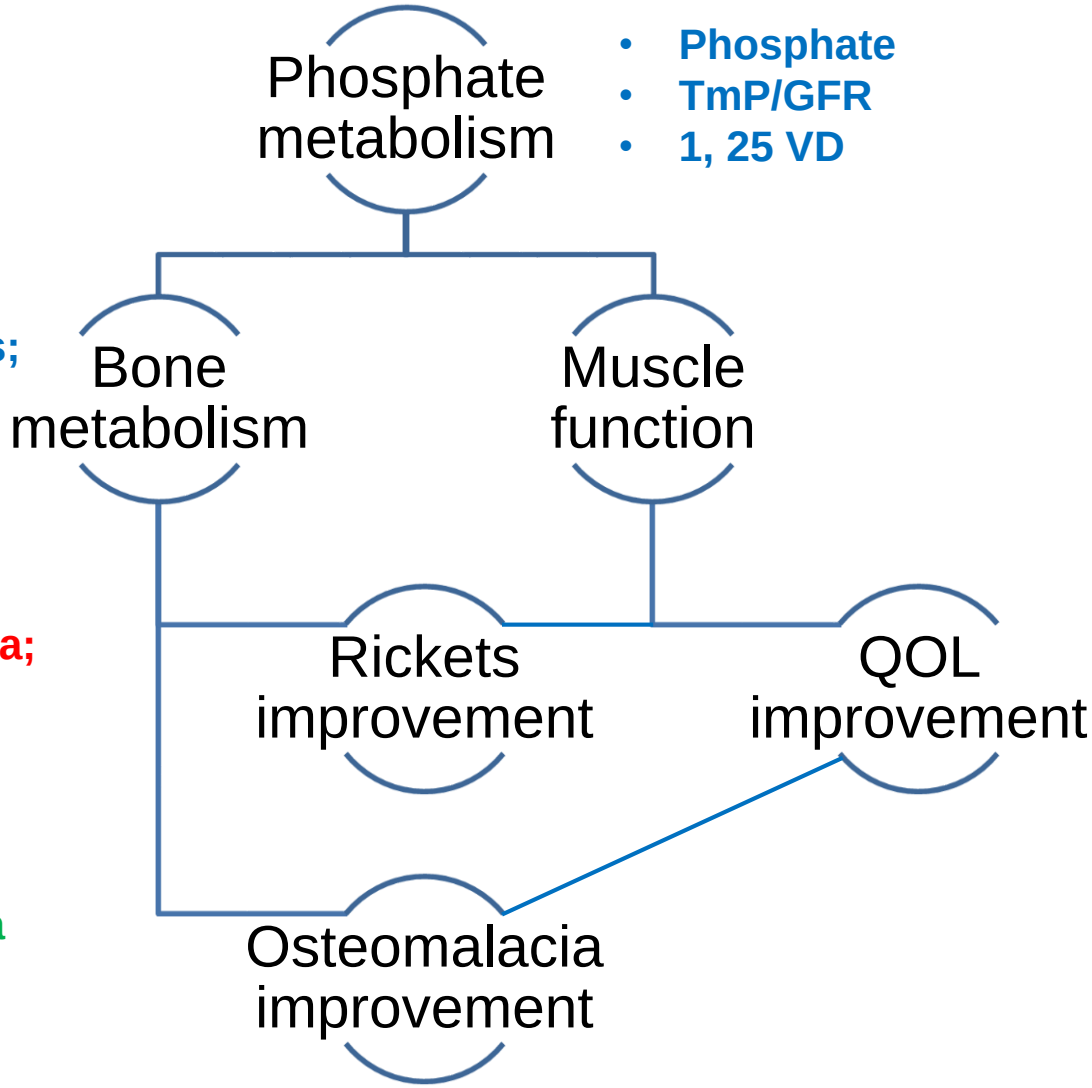

- Phosphate
- TmP/GFR
- 1, 25 VD

- Bone Parameters; ALP, P1NP, CTx

- Radiographic data; RSS, RGI-C
- Growth data

- Bone biopsy data
- Fracture data

- Pain
- Physical function
- Stiffness
- Walking 6MWT

Blue: ped./adult
Red: ped. only
Green: adult only

Clinical studies for XLH

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

Clinical Status Updates Summary

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- 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

EU Regulatory Update (1)

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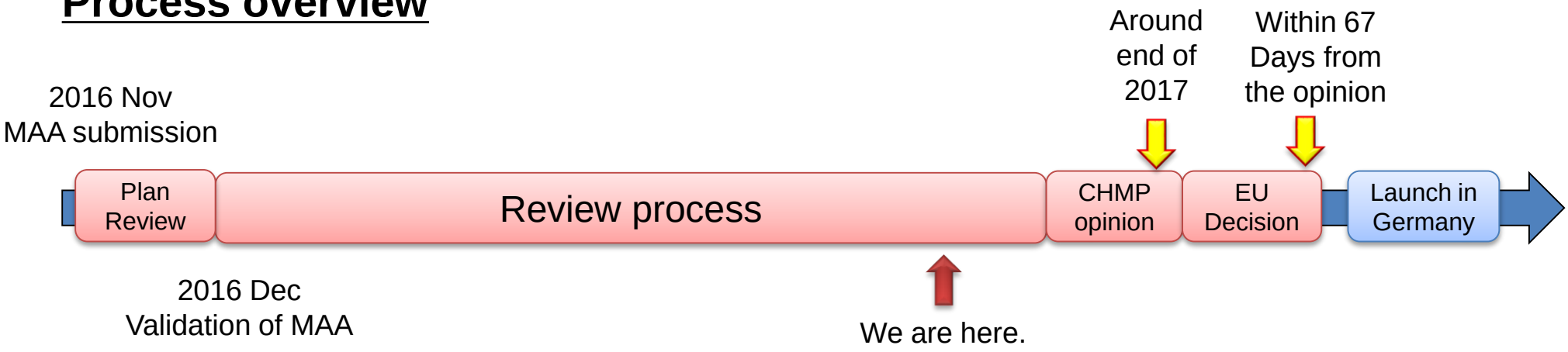
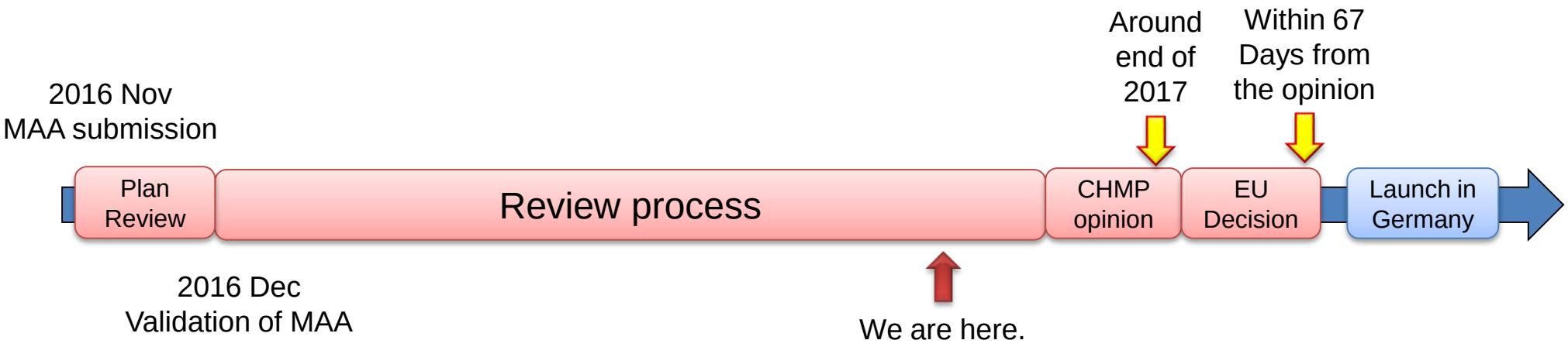
Process overview



- 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.

EU Regulatory Update (2)



- 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)

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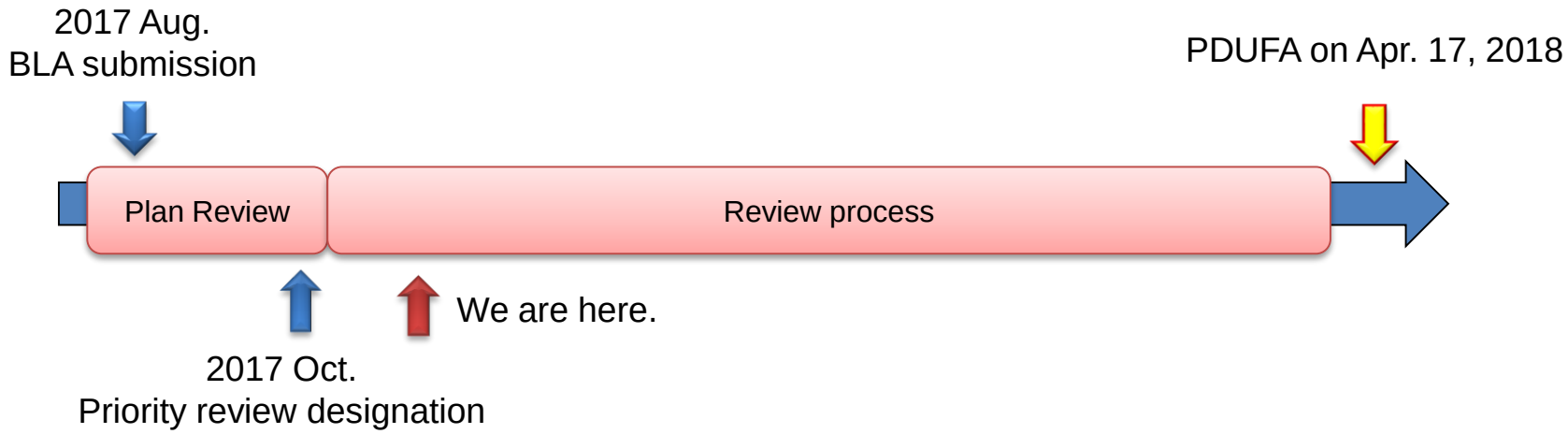
Process overview



- 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

US Regulatory Update (2)

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- 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

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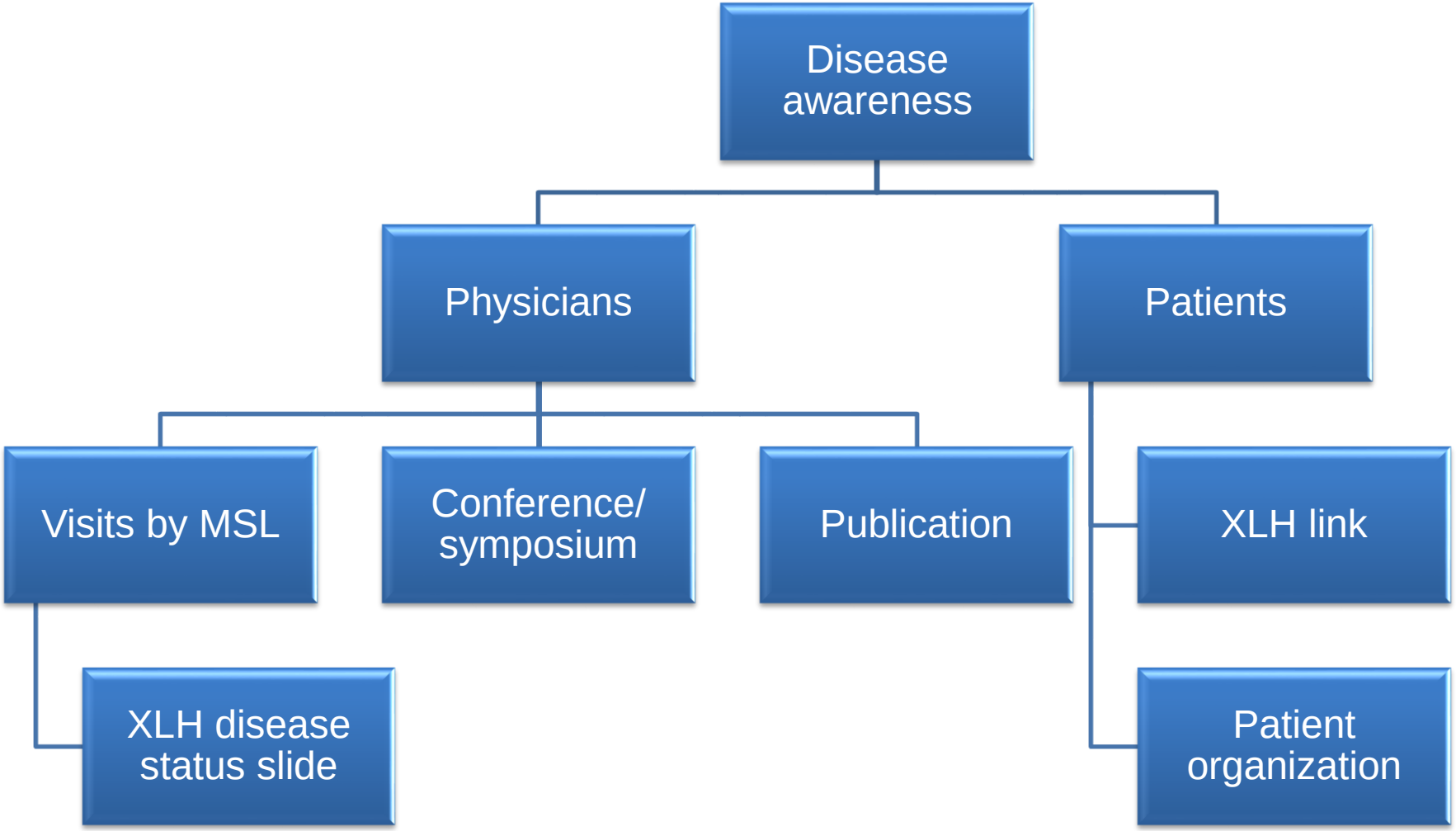
- Commercial organization: Rare Disease Business Unit in KKI
- Disease awareness
- Patient and physician identification
- Branding and Marketing message preparation (not to be used pre-approval)
- Market Access (pricing)
- Supporting an XHL patient community in EU
- XLH Registry and Early access program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

Disease Awareness Activities



Disease Awareness Activities

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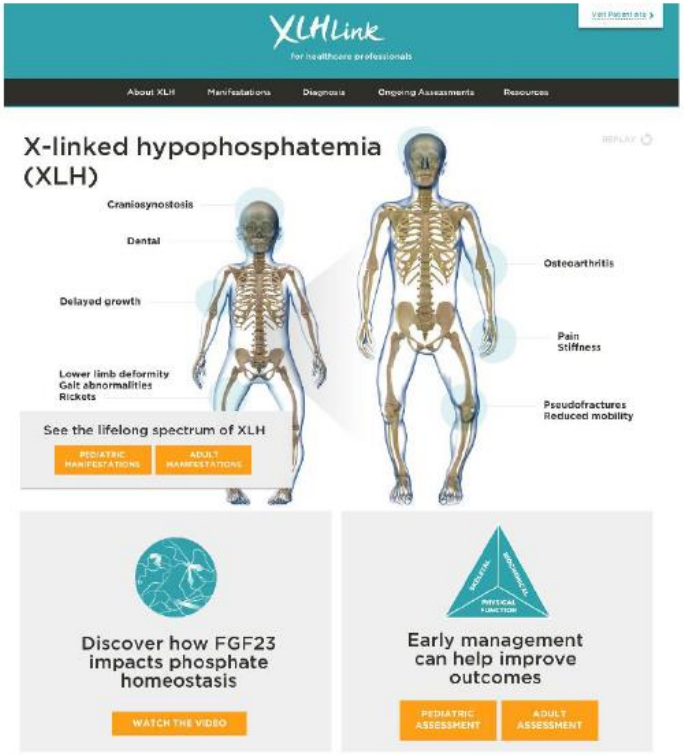
xlhlink.com (for patients)
Launch date 21st Aug 17

- 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

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

Registry and EAP

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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

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