Transforming good science into great medicine for rare diseases

Jefferies Healthcare Conference

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Emil Kakkis, MD, PhD
Chief Executive Officer and President
Legal Warning

- **Cautionary note regarding forward-looking statements**: The following information contains forward-looking statements, including statements regarding our expectations regarding the timing of reporting results from our clinical studies of KRN23, rhGUS, and triheptanoin (in LC-FAOD and Glut1 DS); our expectations regarding the timing of commencing clinical studies with respect to KRN23 and Ace-ER and completing enrollment for our Phase 3 study of rhGUS; our expectations regarding support of planned investigator-sponsored trials; the design of studies for our product candidates; the likelihood of regulatory approvals for our product candidates; our expectations regarding pursuit of conditional approval for KRN23 and Ace-ER; the potential market opportunities for commercializing our product candidates; our plans to commence named-patient sales; our expectations regarding the potential market size and the size of the patient populations for our product candidates, if approved for commercial use; our intentions regarding business and commercial development; our estimate regarding the ability of existing cash to fund current operating plans; and other similar statements. Any forward-looking statements made by us reflect our current views with respect to future events or to our future financial performance and involve known and unknown risks, uncertainties, and other factors that may cause our actual results, performance, or achievements to be materially different from any future results, performance, or achievements expressed or implied by these forward-looking statements. Accordingly, our actual results may materially differ from our current expectations, estimates, and projections. Given these uncertainties, you should not place undue reliance on these forward-looking statements.

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Ultragenyx Pharmaceutical Inc.
A rare disease company by design

• Founded in 2010, IPO in 2014
• Focused on serious metabolic genetic disorders
• Six clinical programs in Phase 2 or later
• Proven team with expertise in rare disease
• Well financed with cash to fund operations into 2018
Business Strategy for Maximum Efficiency
Focus resources on the clinical data engine

• Select genetic diseases with clear biology
  – Higher probability of success

• Translate existing science to clinic rapidly
  – Modest investment in early-stage research

• Develop both small molecules and biologics
  – Reduced overall investment in manufacturing

• Utilize contract manufacturing only
  – Lower investment in facilities and people
# Ultragenyx Pipeline

Developing multiple clinical-stage programs in parallel

<table>
<thead>
<tr>
<th>Candidate</th>
<th>Description</th>
<th>Indication</th>
<th>Pre-clinical</th>
<th>Phase 1</th>
<th>Phase 1/2 or Phase 2</th>
<th>Phase 3 or Pivotal</th>
<th>Ultragenyx Commercial Rights</th>
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<tbody>
<tr>
<td>KRN23</td>
<td>Anti-FGF23 monoclonal antibody</td>
<td>XLH</td>
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<td>U.S. and Canada: Joint with KHK¹ (profit share)</td>
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<td>(UX023)</td>
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<td>KRN23</td>
<td>Anti-FGF23 monoclonal antibody</td>
<td>TIO</td>
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<td>U.S. and Canada: Joint with KHK (profit share)</td>
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<td>rhGUS</td>
<td>Enzyme replacement</td>
<td>MPS 7</td>
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<tr>
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<td>Enzyme replacement</td>
<td>Galactosialidosis</td>
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<td>Substrate replacement</td>
<td>LC-FAOD</td>
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<td>Glut1 DS</td>
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<td>Worldwide</td>
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<td>Ace-ER</td>
<td>Substrate replacement</td>
<td>GNE Myopathy (HIBM)</td>
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<td>Worldwide (excluding Japan and certain other Asian territories)</td>
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¹Kyowa Hakko Kirin

| Biologic     | Small Molecule                |
Phase 2 fully human monoclonal antibody against FGF23 (SC injection)

KRN23 for X-Linked Hypophosphatemia* (XLH)

*Also known as X-linked hypophosphatemic rickets or vitamin D-resistant rickets
KRN23 MAb Against FGF23 for XLH
Increases low serum phosphate associated with bone disease

**XLH**: Excess FGF23\(^1\) causes excess renal phosphate loss

**Key symptoms**: Rickets, deformity, short stature; fractures, pain, and stiffness in adults

**Standard of care**: Oral phosphate + Vitamin D (nephrocalcinosis risk)

**US prevalence**: ~12,000

**Clinical data**: 16-month adult Phase 1/2 showed increased serum phosphate\(^2\)
Phase 1/2 Data in Adults
KRN23 increased phosphate in adults for up to 16 months

- Study Design
  - Open-label in adults with XLH
  - Monthly subcutaneous injection

- Efficacy
  - Serum phosphate increased in all patients
  - Majority of patients reached normal phosphate range at peak over 12 months

- Safety
  - Generally safe and well-tolerated

ICE/ENDO June 2014 and ASBMR September 2014
Pediatric Phase 2 Study Ongoing
Phosphate data released Q215; rickets data expected ~YE15

**Study Design**

- **Study Design**
  - *Q2 Week Dose Group*
    - Titration Period: 16 weeks
    - Treatment Period: 48 Weeks
  - *Q4 Week Dose Group*
    - Titration Period: 16 weeks
    - Treatment Period: 48 Weeks

- **Efficacy Endpoints**
  - **Thacher Rickets Severity Scale (RSS)**
  - RSS: 10-point scale of knee and wrist irregularities
  - Height growth velocity

- **N = 36 patients enrolled, ages 5-12y**
- 16-week data reported June 2015 (phosphate control and safety)
- 40-week data on bone/growth late 2015 / early 2016
Pediatric Phase 2 Interim Results

Phosphate levels increased in all patients at 16-weeks

**Monthly Dosing Group**
- 71% of patients in normal range at peak at 16 weeks
- Of patients who reached week 22, 9 out of 12 (75%) in normal range after further titration

**Biweekly Dosing Group**
- 50% of patients in normal range at 16 weeks
- Of patients who reached Week 24, 7 of 9 (78%) in normal range after further titration

**Phosphate Change with Standard of Care (SOC)**
- Data available for 16 patients on SOC at screening before washout
  - On SOC at screening: 2.40 mg/dL = +0.14 mg/dL over baseline
  - After 16 wks KRN23: 3.09 mg/dL = +0.83 mg/dL over baseline
Pediatric Phase 2 Other Results and Safety
Consistent increases in metabolic markers; safe and well-tolerated

<table>
<thead>
<tr>
<th>Other Metabolic Measures</th>
<th>Safety &amp; Tolerability</th>
</tr>
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<tbody>
<tr>
<td>• Increases in TmP/GFR consistent with serum phosphate and comparable to adult data</td>
<td>• No SAEs or discontinuations</td>
</tr>
<tr>
<td>• Serum 1,25 Vitamin D rises consistent with phosphate data</td>
<td>• Most common AEs were injection site-related</td>
</tr>
<tr>
<td>• Dose-response in pediatric study consistent with adult XLH data generated to date</td>
<td>• No significant changes in serum calcium, urinary calcium, iPTH</td>
</tr>
<tr>
<td></td>
<td>• No serum phosphate above the normal range</td>
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</table>
KRN23 Regulatory Status for XLH
Accelerating the program with possible conditional EU pathway

• Conditional approval possibility in Europe
  – Feedback from EMA indicates conditional approval filing may be possible based on ongoing pediatric and adult studies
  – Planning to expand pediatric Phase 2 by up to 16 patients
  – Decision to file based on 40-week rickets data from pediatric Phase 2 around YE 2015 (original 36 patients) or mid-2016 (expanded, n~50)

• Adult Phase 3 program to begin in 2015
  – Expect to initiate 48-week pivotal adult program based on discussions with FDA and EMA
  – Phase 3 randomized, double-blind, placebo-controlled study with serum phosphate as primary endpoint (n=120)
  – Open-label study evaluating bone quality/osteomalacia (n=10)
KRN23 for Tumor-Induced Osteomalacia* (TIO)

New program for fully human monoclonal antibody against FGF23 (SC injection)

*Also known as oncogenic hypophosphatemic osteomalacia or oncogenic osteomalacia
KRN23 MAb Against FGF23 for TIO
Intended to block FGF23 over-expressed by tumors

• **TIO**: Benign tumors cause excess FGF23 and hypophosphatemia

• **Severe XLH-like disease**: Severe osteomalacia, fractures, pain, muscle weakness

• **Standard of care**: Resection of tumors (~50% of cases); oral phosphate

• **US prevalence**: ~500-1,000

• **Clinical data**: Phase 2 ongoing
  – Profound effect of tumor resection supports anti-FGF23 biology

[Image: Bone scan (Front) (Back)]
Study Design

- N = 6 inoperable patients
- Interim data expected late-2015
- Status: currently enrolling and dosing patients

Endpoints

- Dose, regimen, and safety
- Radiographic assessments, muscle strength, walking, and QOL
- Biopsy, bone markers, phosphate, and other biochemical measures
Recombinant Human β-glucuronidase (rhGUS) for Mucopolysaccharidosis 7 (MPS 7): Sly Syndrome

Phase 3 enzyme replacement therapy (IV infusion)
rhGUS ERT in MPS 7: Sly Syndrome
Symptoms and ERT treatment similar to other MPS diseases

• MPS 7: Glycosaminoglycans (GAG) storage caused by enzyme deficiency

• Key symptoms/prognosis
  – Large liver/spleen, airway/pulmonary disease, joint stiffness, etc.
  – Death: teens-30s; hydrops¹ < 1 year

• Treatment: No approved drug therapy

• Prevalence: ~200 patients worldwide

• Clinical data: Reduction in urinary GAG excretion and liver size and no drug-related SAEs and IARs²

¹ Non-immune hydrops fetalis, a very severe neonatal condition
² SSIEM 2014
rhGUS Phase 3 Study Initiated Q414
Agreement reached with FDA and EMA on pivotal study design

Blind-Start Study Design

- Phase 3 enrollment ongoing
- Phase 3 data expected first half of 2016

Efficacy Endpoints

- FDA: No primary; totality of data to be reviewed
- EMA: Urinary GAG primary

Urinary GAG Decline in Phase 1/2

- Multiple clinical secondary endpoints
Triheptanoin for Long-Chain Fatty Acid Oxidation Disorders* (LC-FAOD)

Phase 2 substrate replacement therapy (oral liquid)

*Includes VLCAD, LCHAD, CPT-I, CPT-II, TFP, CACT
Triheptanoin for LC-FAOD
Triglyceride of C7: alternative energy source to long-chain fat

- **LC-FAOD**: Inability to convert fat into energy
- **Key symptoms/prognosis**
  - Hypoglycemia, muscle rupture, heart failure
  - Mortality of ~50%; a cause of SIDS
- **Standard of care**: Diet and MCT oil
- **US prevalence**: ~2,000 – 3,500
- **Clinical data**: ~13 years of study suggest reduction in major medical events

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2. Medium chain triglycerides  
3. Vockley SSIEM 2013
Phase 2 Study Reached Target Enrollment
Evaluating effect of triheptanoin on major symptom groups

**Study Design**

- **Run-in (4 weeks)**
  - Maintain Current Therapy

- **24 Week Treatment Period**
  - Visits Q 4-6 weeks

- **24-Week Primary Analysis**

- **54 Week Extension Period**
  - Visits Q 12-18 weeks

- **Initiate triheptanoin**
  - MCT oil discontinued if applicable

**Efficacy Endpoints**

**Musculoskeletal**
- Exercise tolerance
- Cycle ergometry, 12MWT
- Muscle strength, CK levels
- Rhabdomyolysis events

**Liver**
- Hypoglycemia interventions
- Hepatomegaly
- Major medical events

**Heart**
- Cardiac function/size
- Cardiomyopathy events

- **N = 29** severe subjects enrolled
- **4 genetic types, 3 clinical problems**
- Evaluate at **6 months for acute effects, 18 months for major events**
- Interim data for acute effects expected in second half of 2015
Triheptanoin for Glucose Transporter Type 1 Deficiency Syndrome (Glut1 DS)

Phase 2 substrate replacement therapy (oral liquid)
Triheptanoin for Glut1 Deficiency Syndrome
Alternative energy source for the brain

• **Glut1 DS**: Glucose transport defect causes brain energy deficiency

• **Key symptoms**: Seizures, movement disorder, developmental delay

• **Standard of care**: Ketogenic diet (70-80% of calories in fat, <10% carbs)

• **U.S. prevalence**: ~3,000 – 7,000

• **Clinical data**: Investigator study\(^1\) demonstrated activity in absence seizures and cognitive performance

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\(^1\)JAMA Neurology 2014

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Less Glucose Uptake (red color) in Glut1 DS

Normal Glucose Uptake

Glut1 DS Glucose Uptake

Ann Neurol 2002
Investigator Study in Absence Seizures
Decline in absence seizures and improved cognitive function

- Independent investigator study in 14 patients not on ketogenic diet
- Seizure rate declined in all patients who underwent EEG analysis (n=11)
- Increases in neuropsychological performance
  - As measured by standardized vocabulary tests EVT-2 and PPVT-4
  - After 3 months, 7 of 8 patients on each test had improved from baseline (EVT-2: p=0.02; PPVT-4: p=0.04)
- No serious adverse events observed

Seizure Rate

Neuropsychological Performance

Expressive Vocabulary Test (EVT) and Peabody Picture Vocabulary Test (PPVT) at baseline, 60 minutes, and 3 mos.

1 JAMA Neurology 2014
Glut1 DS Phase 2 Seizure Study Ongoing
Evaluating multiple seizure types

Study Design

Efficacy Endpoints

• Generalized/partial tonic-clonic seizures (patient diary)
• Absence seizures (EEG)
• Cognitive function
• Movement disorder

- N = Up to 40 patients
- Entry requires generalized/partial or absence seizures
- Enrollment still ongoing
- Interim data expected in second half of 2015
Positive Data in Glut1 Movement Disorders
Substantial reduction in paroxysmal events presented at AAN\textsuperscript{1}

- Investigator-sponsored trial in six Glut1 patients with non-epileptic paroxysmal manifestations
- Other improvements observed
  - Clinical global impression scale
  - Normalization of induction of brain energy metabolism
- Triheptanoin was well tolerated
- Company-sponsored trial planned
  - Intend to discuss with regulators in 2H15

\textsuperscript{1}Mochel, Emerging Sciences Session, American Academy of Neurology, April 2015.
Aceneuramic Acid Extended Release (Ace-ER) for GNE Myopathy (GNEM)*

Phase 3 substrate replacement therapy (oral tablet)

*Also known as hereditary inclusion body myopathy (HIBM), distal myopathy with rimmed vacuoles (DMRV), Nonaka disease
Ace-ER Substrate Replacement for GNEM
Sialic acid deficiency leads to progressive muscle atrophy

• **GNE Myopathy**: Sialic acid deficiency

• **Key symptoms**: Irreversible loss of upper and lower muscle function

• **Standard of care**: No approved therapy

• **Prevalence**: ~2,000 worldwide

• **Clinical data**: Slowed upper extremity disease progression over 2 years\(^1\)

\(^1\)World Muscle Society 2014
Ace-ER Phase 2 Results
Upper extremity strength stabilized over 48 weeks

Upper Extremity Composite (UEC) Change

<table>
<thead>
<tr>
<th></th>
<th>6g vs Placebo (24 weeks)</th>
<th>Combined 6g vs Combined 3g (48 weeks)</th>
<th>Combined 6g vs Combined 3g (48 weeks)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Predefined subset</td>
<td>n/a</td>
<td>n/a</td>
<td>≥200M walking at baseline</td>
</tr>
<tr>
<td>UEC Change</td>
<td>+2.33 kg (+5.5%)</td>
<td>+3.44 kg (+8.5%)</td>
<td>+4.69 kg (+9.6%)</td>
</tr>
<tr>
<td>P-value</td>
<td>0.040</td>
<td>0.0033</td>
<td>0.00055</td>
</tr>
</tbody>
</table>

- Lower extremity showed similar pattern
- Positive trend in patient-reported outcomes of functional activity
- No treatment-related SAEs; some GI AEs
- In extension study, appeared to slow projected 2-year UEC loss

1AAN 6/30/14 and WMS 10/11/14
Phase 3 Initiated in May 2015
Data expected in the second half of 2016

Study Design

- 6g/day Ace-ER for 48 weeks (n = 40)
- Placebo for 48 weeks (n = 40)

Randomization

- N = ~80 patients
- ≥200M 6MWT at baseline
- Primary: UEC muscle strength
- Key secondary: GNEM-FAS, lower extremity strength/function

UEC Muscle Strength Primary

- Shoulder Abduction
- Grip
- Elbow Extension
- Elbow Flexion
Pursuing Conditional Approval in Europe
Accelerated path to market while conducting Phase 3

• Decision to file follows Scientific Advice discussions with EMA
• Based on positive upper extremity strength data from Phase 2
• Registration process to be concurrent with Phase 3 conduct
• Intend to file MAA in second half of 2015
• Ongoing disease monitoring program enrolling up to 200 patients to better understand natural history of GNE Myopathy patients
# Commercial Development

Planning for first named-patient sales (NPS) in 2015

<table>
<thead>
<tr>
<th>2010-2014</th>
<th>2015</th>
<th>2016+</th>
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<tbody>
<tr>
<td>Comprehensive patient ID and disease sequencing effort initiated</td>
<td>NPS for rhGUS in EU and/or Turkey</td>
<td>Launch Planning</td>
</tr>
<tr>
<td>• GNEM: ~1,000-1,200 of estimated ~2,000 patients identified</td>
<td>Hire Chief Commercial Officer and other key team members</td>
<td>Sales force targeting medical geneticists and other specialists</td>
</tr>
<tr>
<td>• MPS 7: ~100 of estimated ~200 patients identified</td>
<td>Enhanced global patient ID effort</td>
<td>Presence in key major markets (US, Europe, Brazil)</td>
</tr>
<tr>
<td>Market development activities</td>
<td>Initial EU presence</td>
<td>Continued patient ID and diagnosis support</td>
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</table>
Significant Total Target Patient Population

Across three specialties but with medical genetics overlap

Endocrine

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<th>Total</th>
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<tbody>
<tr>
<td>XLH²</td>
<td>48,000</td>
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<tr>
<td>TIO²</td>
<td>2,000-4,000</td>
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Medical Genetics

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<th>Condition</th>
<th>Total</th>
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<tbody>
<tr>
<td>MPS 7</td>
<td>200</td>
</tr>
<tr>
<td>FAOD</td>
<td>8,000-14,000</td>
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Neurology

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<th>Condition</th>
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<td>GNEM²</td>
<td>2,000</td>
</tr>
<tr>
<td>Glut1 DS</td>
<td>12,000-28,000</td>
</tr>
</tbody>
</table>

¹Developed world estimates shown; all but MPS 7 and GNEM are extrapolations of US estimates
²Ultragenyx does not have worldwide rights
Financial Overview

• Cash\(^1\) (Q1 2015): $343 million
• Operating loss (Q1 2015): $21 million
• Cash used in operations (Q1 2015): $18 million
• No debt

Expect existing cash to fund operations into 2018 with current operating plan assuming all programs progress

\(^1\)Cash, cash equivalents, and short-term investments  \(^2\)Net proceeds
### Key Milestones for 2015

Significant progress and data points expected across pipeline

<table>
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<th>1H15</th>
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<td><strong>KRN23</strong></td>
<td>• Adult Phase 3 initiation</td>
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<tr>
<td>✓ Pediatric Phase 2 16-week data (phosphate/safety)</td>
<td>• TIO Phase 2 interim data</td>
</tr>
<tr>
<td></td>
<td>• Pediatric Phase 2 40-week interim data (or early 2016)</td>
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<tr>
<td><strong>rhGUS</strong></td>
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<tr>
<td>✓ Phase 1/2 36-week data at LDN World</td>
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<tr>
<td><strong>Triheptanoin</strong></td>
<td>• Phase 2 FAOD interim data</td>
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<tr>
<td>✓ Pilot HD IST Data Q1</td>
<td>• Phase 2 Glut1 DS interim data</td>
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<tr>
<td>✓ Pilot Glut1 Motor Data Q2</td>
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<tr>
<td><strong>Ace-ER</strong></td>
<td>• EMA MAA filing</td>
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<tr>
<td>✓ Phase 3 initiation</td>
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*Pivotal data in 2016*
Investment Thesis for Ultragenyx
A rare disease company by design

• Proven rare disease track record for development
• Efficiently transforming unrecognized science into effective rare disease products
• Deep and diversified product pipeline
• Rich set of value drivers in six programs
• A next-generation rare disease company