COMPANY NOTE

Initiating Coverage

USA | Healthcare | Biotechnology

September 23, 2014

Jefferies

Ultragenyx (RARE)

Heading Towards Rarefied Air - Initiate at Buy

BUY

Price target $74.00

Price $54.19

EQUITY RESEARCH AMERICAS

Key Takeaway

We expect RARE's stock to reflect the successful progress and evolution of the drugs in its pipeline into 2017/2018, after which we expect RARE to transform into more of a commercialization story. At this point, we believe mgmt's strong track record of execution in this space will drive continued success. Triheptanoin's prelim phase 2 data Mid-15 could be a major catalyst; we believe its mechanism is uniquely differentiated vs. currently available options.

Leveraging core advantages of the orphan disease business model. With a broad and diversified pipeline, we believe RARE will establish itself as the leader in the treatment of ultra-rare severe metabolic genetic diseases. Management has successfully executed on several clinical programs like rhGUS for MPS 7, KRN23 for XLH, and SA-ER for HIBM in 2014.

Triheptanoin's (THN's) unique mechanism of action could differentiate it vs. other diet options; could be a pipeline in itself. We view THN's mechanism of action as a clear advantage over other options as it provides the optimal ratio of molecules to perpetuate the TCA cycle and maintain a constant energy level in patients suffering from LC-FAODs and Glut 1 DS. This has been corroborated by initial data, and we believe preliminary ph 2 data in Mid-15 could be a major catalyst (~$690M peak WW adjusted sales) potentially setting the stage for expansion into other metabolic and/or mitochondrial disorders.

SA-ER higher dose and extension data at WMS mtg, Oct 11. While the 48 week data so far has been encouraging, we believe prelim. data with the 12g higher dose (including 6g immediate release for quicker absorption) in 10 treatment naïve patients and extension study patients could provide an upside surprise prior to initiating a registration study.

Impressive data for KRN23 in adults. KRN23 is another drug with a clean mechanism that has had solid ph 2 proof-of-concept data in XLH adults, which we believe will be replicated in the pediatric phase 2 study. We expect initiation of a ph 3 study in pediatrics in 2H15 after prelim. ph 2 data and forecast peak WW adjusted revenues to RARE of $295M.

rhGUS phase 3 study to initiate by YE14. RARE has buy-in from the EMA on the ph 3 design but continues discussions with the FDA on use of uGAG levels as the primary endpoint. With supportive data and several ERTs already approved we expect rhGUS to be RARE's first commercial drug.

Valuation/Risks

Our $74 PT is DCF-based. Risks include clinical, regulatory, competitive, commercial.

Financial Summary	
Net Debt (MM):	$0.0
Cash & ST Invest. (MM):	$162.6

Market Data	
52 Week Range:	$69.77 - $32.02
Total Entprs. Value (MM):	$1,717.8
Market Cap. (MM):	$1,717.8
Insider Ownership:	31.3%
Institutional Ownership:	70.7%
Shares Out. (MM):	31.7
Float (MM):	21.3
Avg. Daily Vol.:	452,155

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USD	*Prev.*	2013A	*Prev.*	2014E	*Prev.*	2015E	*Prev.*	2016E
Rev. (MM)	--	0.0	--	0.0	--	0.0	--	0.0
EPS								
Mar	--	--	--	(0.63)A	--	--	--	--
Jun	--	--	--	(0.45)A	--	--	--	--
Sep	--	--	--	(0.44)	--	--	--	--
Dec	--	--	--	(0.44)	--	--	--	--
FY Dec	--	(10.37)	--	(1.74)	--	(2.30)	--	(2.56)
FY P/E		NM		NM		NM		NM

Price Performance

Ultragenyx Pharmaceuticals

BUY: $74.00 Price Target

THE LONG VIEW

Scenarios

Target Investment Thesis

- For the following programs, we project the following launch years and peak WW probability adj. revenues:
  THN (LC-FAOD) – 2018/$328M
  THN (GLUT1 DS) – 2018/$363M
  rhGUS – 2017/$57M
  SA-ER – 2018/$65M
  KRN23 – 2018/$295M in revs to RARE
- We do not assign any value to **rhPPCA** (preclinical)
- DCF-based PT: $74

Upside Scenario

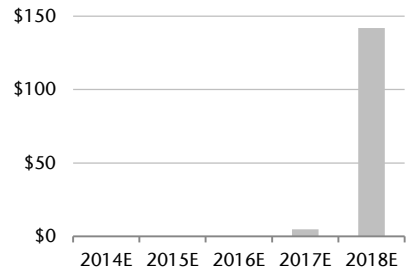
- KRN23 and rhGUS maintain their market share post patent expiration
- DCF-based PT: $101

Downside Scenario

- Triheptanoin fails to demonstrate clinically meaningful data for GLUT1 DS patients.
- SA-ER fails in a registration study
- DCF-based PT: $45

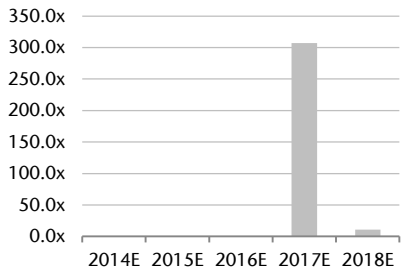
Long Term Analysis

Revenue (M)



Source: Factset & Jefferies

Enterprise Value (EV)/Revenue



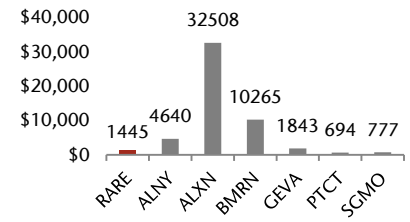
Source: Factset & Jefferies

Other Considerations

We believe there is significant opportunity for RARE to continue to in-license products and sustain long-term growth

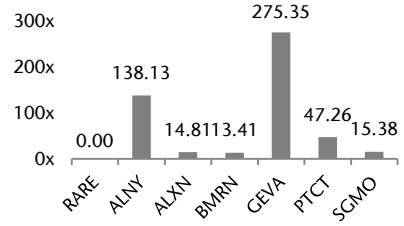
Peer Group

Enterprise Value (EV)



Source: Factset

Enterprise Value (EV)/Revenue



Source: Factset

Recommendation / Price Target

Ticker	Rec.	PT
RARE	**Buy**	**$74.00**
ALNY	NC	NC
ALXN	Hold	$156.00
BMRN	Buy	$84.00
GEVA	NC	NC
PTCT	NC	NC
SGMO	Buy	$22.00

Catalysts

- SA-ER – interim data for SA-ER at WMS (10/11/14)
- rhGUS – initiate phase 3 trial – YE14
- THN – interim phase 2 data in LC-FAOD & GLUT1 DS – Mid-15
- KRN23 – interim phase 2 data in pediatric patients – 2H15

Company Description

Ultragenyx (RARE) is a development stage biotech company that is focused on developing and commercializing a broad pipeline of biologics (monoclonal antibody and enzyme replacement therapies) and small molecules (substrate replacement therapies) for the treatment of rare and ultra-rare serious metabolic genetic diseases. RARE has built its pipeline via in-licensing resulting in four clinical candidates for five indications: Triheptanoin/UX007 (THN) as an alternate source of energy for patients with long chain fatty acid oxidation disorders (LC-FAOD) and for patients with glucose transporter type 1 deficiency syndrome (Glut1 DS); KRN23 (in collaboration with Kyowa Hakko Kirin) for the treatment of X-linked hypophosphatemia (XLH); rhGUS for MPS VII (e.g. Sly Syndrome); and Sialic Acid Extended release for hereditary inclusion body myositis (HIBM).

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Executive Summary

We are initiating coverage of Ultragenyx Pharmaceuticals (RARE) with a Buy rating and a YE15 price target of $74. RARE is an orphan disease company that has very rapidly built a broad and simultaneously diversified pipeline of in-licensed drugs. RARE's business model is a core advantage as is evident through its specific focus on rare and ultra-rare diseases, drugs with a clear mechanism of action/biology, its relationships with the rare disease community/treating physicians, and commercial leverage globally (all drugs could launch in the 2017-2018 timeframe). This ultra-orphan focus was borne out in the company's ability to in-license multiple drugs for severe metabolic diseases from a mix of academia and corporates over a short period of time since its founding in 2010. Other key advantages include shorter development timelines (time and cost-efficient; early proof-of-concept), capital efficiency, pricing power, and orphan exclusivity – all potentially contributing to profitability relatively quickly after commercial launch.

The two small molecules in RARE's pipeline are Sialic acid-extended release (SA-ER) in phase 2 for the treatment of Hereditary Inclusion Body Myositis (HIBM) and Triheptanoin (THN) in phase 2 for the treatment of long chain fatty acid oxidation disorders (LC-FAOD) and glucose transporter type 1 deficiency syndrome (Glut1 DS). SA-ER data has been met with a healthy level of skepticism so far. However, we think sentiment could change if the higher dose being studied (12g, including 6g immediate release to take advantage of more efficient absorption in the stomach; this should theoretically increase SA levels in muscle) has a positive impact on upper/lower extremity muscle strength for the 10 treatment naïve patients and/or in patients in the 36 week extension phase. Preliminary data from the treatment naïve patients and the extension phase is expected to be presented at the World Muscle Society meeting on Oct 11. In the event the 12g dose is not successful, we believe RARE could still have a path forward with the 6g dose in patients with less advanced disease at baseline (in whom SA-ER has demonstrated a pronounced improvement) and with upper extremity muscle strength as a primary endpoint pending regulatory approval. RARE believes the FDA could be open to approving drugs on muscle strength if these improvements are clinically relevant. Additionally, RARE is working to identify HIBM patients by providing free genetic screening to patients with uncharacterized myopathies, and also participating in collaborative patient-screening with other companies focused on muscle myopathies/limb girdle dystrophies where there is no clear cause. We forecast adjusted peak WW sales of ~$65M.

THN is the key value driver for the stock longer-term and interim data from the two phase 2 trials is expected in mid-15. THN has two important characteristics that make it ideal for solving metabolic disorders such as LC-FAOD/GLUT1 DS: 1) its size allows it to enter normally restricted compartments like the mitochondria and the brain; and 2) each THN molecule is metabolized into the unique and optimal ratio of 2 units acetyl-CoA (A-CoA) to 1 unit of propionyl-CoA (P-CoA). With these features, THN can perpetuate the TCA cycle (a.k.a. Kreb's cycle) throughout the body (the central metabolic process for providing cellular energy) and provide substrate for neurotransmitter production in the brain. LC-FAOD is characterized by a deficiency in long chain fatty acid metabolism that leads to insufficient energy production via the TCA cycle. There is a clear unmet need for a more effective therapy as current treatments like high carbohydrate diets and medium chain triglycerides (MCT) oil do not supply the correct fuel to keep the TCA cycle going, which results in periods of insufficient cellular energy and build-up of toxic by-products. We forecast adjusted peak WW sales of ~$328M for THN in LC-FAOD patients. Glut1 DS patients have an impaired ability to transport glucose across the blood/brain barrier. While a ketogenic diet (KD) can alleviate some seizures and

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movement disorders in GLUT1 DS patients, it has a minimal effect on other neurological symptoms like impaired cognition and brain maturation. KD provides inadequate raw materials for the production of TCA cycle intermediaries and neurotransmitter, which leads to its lack of effectiveness. Additionally, compliance with KD, particularly in children, is difficult due to the high levels of fat and lack of carbohydrates. Again, THN is superior as it allows perpetuation of the TCA cycle and adequate neurotransmitter biosynthesis with potential for a cognitive benefit. We forecast adjusted peak WW sales of ~$363M for THN in GLUT1 DS patients. We believe the opportunity for THN extends beyond these initial indications, with the potential to expand into other orphan/ultraorphan energy metabolism and mitochondrial diseases associated with genetic defects in pyruvate metabolism and other components of the TCA cycle.

KRN23 (monoclonal antibody to FGF23) and rhGUS (enzyme replacement therapy) are the two biological drugs in RAREs pipeline. KRN23 is an antibody to FGF23 for the treatment of X-linked hypophosphatemia (XLH) being developed in collaboration with Kyowa Hakko Kirin (KHK). KRN23 has a clean mechanism of action and has produced solid clinical data so far. The proof-of-concept for KRN23 was recently presented in the phase 1/2 adult repeat dose study where serum phosphate (Pi) and Vitamin D were increased after multiple doses. We view the repeat dose data as de-risking some key safety concerns including the potential for anti-KRN23 antibodies and hypercalcemia. No patients experienced serum Pi > 4.5 mg/dL which is critical given that the formation of phosphate precipitates requires sustained serum Pi's of 7-8 mg/dL. While the data presented was in adults, RARE's initial focus for KRN23 development will be in pediatric patients who would have the greatest potential for improvement and would stand to benefit from early intervention. We believe the interim clinical data including blinded radiographic assessments of bone disease after 24 weeks of treatment in 2H15 should be sufficient for initiation of a phase 3 study in pediatric XLH patients. A phase 2b study in adults is also planned to be initiated in parallel. Although KRN23 is partnered with KHK, RARE is entitled to ~30% of the economics. We forecast adjusted peak WW revenues to RARE of ~$295M from both pediatric and adult XLH patients.

rhGUS is an enzyme replacement therapy for MPS VII or Sly syndrome that is in a phase 1/2 open label study in *5* patients. Recently presented interim 12 week data from 3 patients demonstrated proof-of-concept sustained uGAG reductions from baseline and liver volume decreases. Based on these data and 24 week data on uGAG reductions from an emergency IND patient, RARE will be initiating a phase 3 study with the uGAG endpoint by YE14. We believe the EMA is on board with the uGAG primary endpoint as long as there is a directional benefit on the clinical endpoints, but the FDA may want to see the correlation of these uGAG levels with other clinical endpoints. We expect positive data in the phase 3 trial as ERTs are a proven approach in MPS disorders. Upside could come from the initiation of a study of rhGUS in MPS VII patients < 5 years old including those with hydrops fetalis. We forecast adjusted peak WW revenues of ~$57M.

Valuation

We value RARE at $74/share using a DCF model (forecast period 2015-2030, 35.1M diluted shares outstanding and a 10% discount rate) that includes probability-adjusted WW sales/royalties for THN (FAOD/GLUT1 DS), rhGUS (MPS VII), SA-ER (HIBM) and adjusted revenues to RARE for KRN23 (XLH). We assume rhGUS is launched in 2017 and the rest of the products launch in 2018. We assume the following probabilities for success and WW peak-adjusted revenues for each product: THN for LC-FAOD (70%, ~$328M), THN for GLUT1 DS (60%, ~$363M), rhGUS (70%, ~$57M), and SA-ER (70%, ~$65M). For

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KRN23, we forecast adjusted peak WW revenues to RARE of ~$295M (75% probability). We forecast R&D expenses to grow from ~$42M in 2014 to $75M in 2017, and to remain relatively constant through the outer years (2018+). We estimate SG&A expenses to increase from ~$10M in 2014 to $35M in 2017 to support rhGUS launch, and then grow up to ~$85M by 2020 to support its global sales/marketing team for all of its products. We have assumed an equity financing of $200M at $74 on 2.7M shares in 2016. We forecast 2019 as being the first full year of profitability and a full corporate tax rate of 30% in 2023.

Risks

Clinical: Translating promising data from preclinical models to humans and replicating early stage clinical data in late stage studies presents a significant risk. We would highlight the THN program in Glut1DS, and the SA-ER program in HIBM as pipeline programs falling into this category.

Regulatory: With a diversity of programs in orphan/ultraorphan diseases we expect RARE to use specific, novel, and non-traditional designs after getting regulatory input from the agencies.

Competitive: There are few if any approved alternatives for the orphan diseases that RARE is pursuing outside of dietary, lifestyle , and behavioral modifications, e.g. inorganic phosphate and calcium for XLH; diet, behavior, and MCT oil for FAOD; ketogenic diet and antiepileptics for Glut1 DS; diet for HIBM and MPS VII.

Commercial: The commercial uptake may not meet management expectations due to inability to identify the expected number of patients, slower physician acceptance, patient willingness to go on new therapies, and reimbursement hurdles. Drug pricing has generally been under scrutiny and has included drugs for orphan diseases.

Description

Ultragenyx (RARE) is a development stage biotech company that is focused on developing and commercializing a broad pipeline of biologics (monoclonal antibody and enzyme replacement therapies) and small molecules (substrate replacement therapies) for the treatment of rare and ultra-rare serious metabolic genetic diseases. RARE has built its pipeline via in-licensing resulting in four clinical candidates for five indications. Triheptanoin/UX007, a medium odd chain triglyceride of three seven-carbon fatty acids, is an oral substrate replacement therapy as an alternate source of energy for patients with long chain fatty acid oxidation disorders (LC-FAOD) and for patients with glucose transporter type 1 deficiency syndrome (Glut1 DS). THN is currently in separate phase 2 studies in severe LC-FAOD patients and Glut1 DS patients that have seizures. Interim data from both studies is expected in Mid-15. KRN23/UX023 is a subcutaneous monoclonal antibody that binds FGF23 for the treatment of X-linked Hypophosphatemia (XLH) and is being developed in collaboration with Kyowa Hakko Kirin. RARE recently initiated a phase 2 study in pediatric XLH patients from which interim data is expected in 2H15. RARE has already run a phase 1/2 study in adult patients and expects to initiate a phase 3 study in pediatric patients pending the phase 2 data with a phase 2b study in adults to initiate in parallel. Recombinant human beta-glucuronidase (rhGUS/UX003) is an IV enzyme replacement therapy licensed from St. Louis University for the treatment of MPS VII/Sly syndrome. RARE expects to initiate a phase 3 study by YE14, the design and endpoints for which the EMA has agreed to. SA-ER/UX001 is an oral formulation of sialic acid licensed

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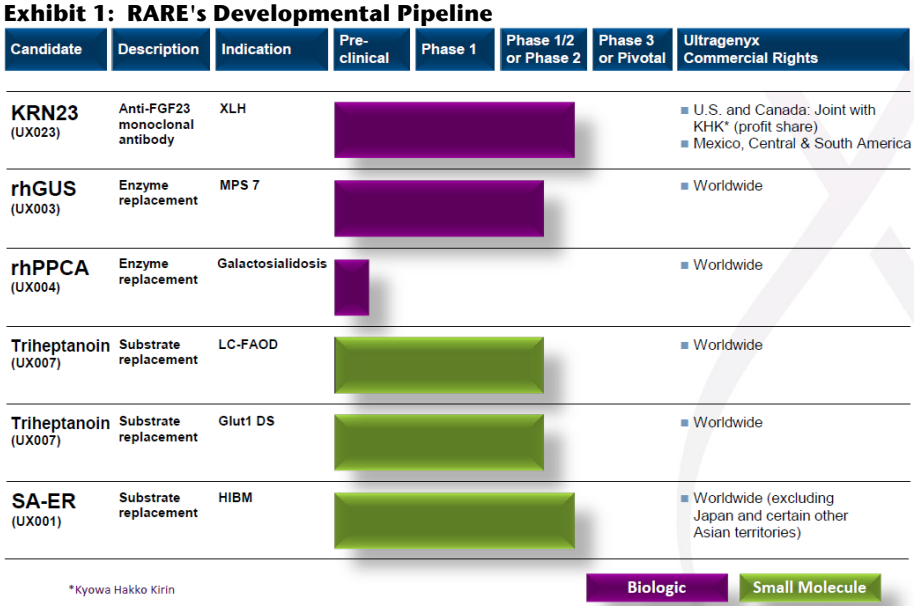
from NobelPharma that is currently in the extension portion of a phase 2 study for the treatment of Hereditary Inclusion Body Myositis (HIBM). Finally, recombinant human protective protein cathepsin-A (rhPPCA/UX004) that was licensed from St. Jude's is an ERT for galactosialidosis in preclinical development.

Pipeline

Exhibit 1: RARE's Developmental Pipeline



Source: Company Data

Catalysts

Exhibit 2: Upcoming catalysts for RARE

				2014	2015				2016	
Drug	**Indication**	**Phase**	**Catalyst**	**2H14**	**1H15**		**2H15**		**1H16**	
				4Q14	1Q15	2Q15	3Q15	4Q15	1Q15	2Q15
KRN23	XLH - Pediatric	II	Interim data							
rhGUS	MPS VII	III	Initiate study	YE14						
THN	GLUT1 Deficiency	II	Interim data			Mid-15				
THN	FAOD	II	Interim data			Mid-15				
SA-ER	HIBM	II	Data at WMS	11-Oct						

Source: Company Data & Jefferies

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KRN23/UX023 – Normalizing phosphate levels for the treatment of X-linked hypophosphatemia (XLH)

KRN23, which is being developed in collaboration with Kyowa Hakko Kirin (KHK), is a recombinant human monoclonal antibody administered via subcutaneous injection that is designed to bind and inhibit fibroblast growth factor 23 (FGF23). FGF23 is an important endocrine signal that contributes to skeletal development and growth by regulating both phosphate homeostasis and vitamin D production. Dysregulation of FGF23 can lead to either increased serum phosphate (hyperphosphatemia), such as in the case of familial tumoral calcinosis, or decreased serum phosphate (hypophosphatemia), such as in X-linked hypophosphatemia (XLH). Binding of KRN23 to FGF23 reduces excess urinary phosphate loss and increases serum phosphate and Vitamin D levels. RARE recently initiated a phase 2 study in pediatric XLH patients from which interim data is expected in 2H15. RARE has already run a phase 1/2 study in adult patients (4 month dose escalation and 12 month extension) and expects to initiate a phase 3 study in pediatric patients by YE14 pending data from the phase 2 study with a phase 2b study in adults to initiate in parallel. In the US and Canada, RARE and KHK will share the profits equally for the first 5 years after which RARE will receive a mid to high 20% royalty (expected to approximate RARE's profit share). In Europe, RARE will receive up to a 10% royalty from KHK and will pay out a low single digit royalty in Latin America given RARE's full ownership of rights in this region. We estimate KRN23 to be launched in the US, Europe, and Latin America in 2018 generating peak worldwide adjusted revenues to RARE of $295M

KHK Collaboration

RARE signed a collaboration and license agreement for KRN23 with KHK in August 2013 covering the treatment of orphan diseases in US/Canada, Europe, and Latin America. Key details of this agreement are outlined in Exhibit 3 below.

Exhibit 3: RARE's partnership agreement with KHK

Key Terms	US and Canada	Europe	Latin America
Commercialization	• Ultragenyx launches • KHK books sales • 50/50 profit share for 5 years • Shared commercial activities	KHK commercializes and books sales	Ultragenyx commercializes and books sales
Royalties	Tiered revenue share in mid to high 20% range to Ultragenyx after profit share period	Up to 10% royalty to Ultragenyx	Low single-digit royalty to KHK
Commercial supply	KHK supplies; price is double-digit percentage of net sales	NA	KHK supplies; price is double-digit percentage of net sales

Source: Company Data

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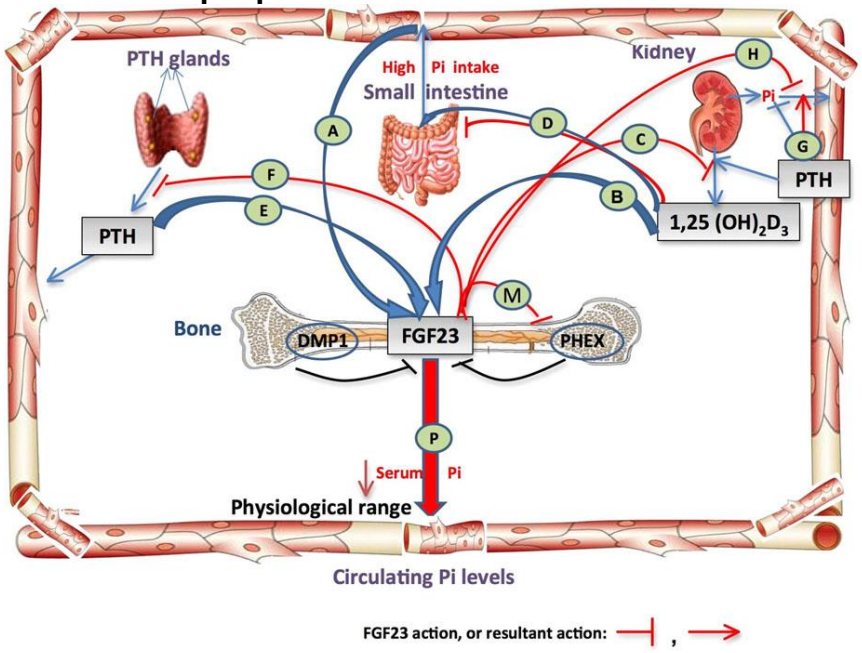
X-linked Hypophosphatemia

Phosphate – biological functions and regulation

Phosphate (Pi or PO_4^{2-}) plays a starring role in some of the most biologically important molecules within our bodies, such as adenosine triphosphate (ATP, the major cellular energy source), nucleic acids (e.g. DNA and RNA), cell membranes and as a structural component of bones and teeth. In fact, up to 85% of the phosphorous in the human body is contained in the bones in the form of a calcium-phosphate salt, known as hydroxyapatite ($Ca_{10}(PO_4)_6(OH)_2$). The control of circulating Pi, and thus what is available for metabolic functions such as bone growth and maintenance, is tightly controlled by several feedback loops between the skeletal system, the parathyroid glands, the kidneys and the small intestines. This system is tightly regulated due to the metabolic importance of Pi and because high levels of Pi can precipitate with calcium in the kidneys (and other soft tissues) potentially leading to nephrocalcinosis (calcium deposits in kidney tissue) and eventually chronic renal failure.

FGF23 is produced by the cells responsible for bone development and maintenance (called osteoblasts) and is the central regulator of Pi. Specifically, FGF23 decreases high serum Pi following dietary absorption by suppressing both the reabsorption of Pi (through inhibition of the activity of the renal sodium phosphate cotransporter protein) and the synthesis of vitamin D in the kidneys (through suppression of the active Vitamin D metabolite calcitriol). When circulating Pi levels return to within a normal range, osteoblasts produce the local signals dentin matrix protein 1 (DMP1) and Phosphate regulating gene with Homology to Endopeptidases located on the X chromosome (PHEX) to prevent continued FGF23 production.

Exhibit 4: Normal phosphate homeostasis



A: High absorbed dietary Pi stimulates FGF23 secretion
B: 1,25(OH)2D3 (Vitamin D) also stimulates FGF23 secretion
C: FGF23 suppresses kidney production of Vitamin D
D: Dietary Pi absorption (which is Vitamin D dependent) is decreased
E: Parathyroid hormone (PTH) also up-regulates FGF23
F: PTH synthesis is decreased by FGF23
G: PTH inhibition of renal reabsorption is decreased
H: Net effect of elevated FGF23 is decreased renal reabsorption of Pi
M: Local bone FGF23 excess results in inhibited mineralization
P: Sum consequence of FGF23 action is to decrease excess Pi to a physiological range
Q: Local skeletal signals PHEX and DMP1 suppress further FGF23 production

Source: Adapted from 'Phosphate homeostasis,' Wikimedia Commons

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XLH pathophysiology

The genetic basis for XLH can be any one of many loss-of-function mutations of the PHEX gene, which in turn removes the ability to downregulate FGF23. As a net result, individuals suffering from XLH have high circulating FGF23 levels, low serum Pi (hypophosphatemia) and low vitamin D. These mutations have been characterized as dominant and therefore affect both males and females alike (although some research suggests that there may be a gene-dosage effect whereby symptoms are worse in males). Current estimates place the prevalence of XLH at 1-9 per 100,000 people, with approximately 3,000-4,000 pediatric and 9,000-10,000 adult patients currently suffering from XLH in the US.

Symptoms of XLH typically appear very early in life including: lower limb deformities, waddling gait, short stature or slow growth rate, spontaneous tooth abscesses, bone pain and potentially muscle pain and weakness. If symptoms are recognized early (parents and pediatricians may attribute signs to 'bulky diapers' or growing pains), initial diagnosis may be nutritional rickets (a dietary deficiency in vitamin D). Vitamin D supplementation on its own has no effect on XLH, thus coining the initial term "Vitamin D Resistant Rickets." Dysregulated Pi is determined by a urinalysis/blood analysis of phosphate levels to calculate both the kidney reabsorption rate of Pi (TRP) as well as the maximum kidney threshold for Pi (TMP/GFR). This clinical finding may then be characterized as XLH by a genetic screen. ~66% of pediatric patients have a familial history of XLH and are identified by blood/urinalysis at birth while the rest are identified by the bowing of their legs when they begin to walk. If left untreated, consequences of XLH include abnormal long bone growth (e.g. the typical bow-leggedness associated with rickets), short stature and osteomalacia (unmineralized bone tissue). Progressing into adulthood, XLH patients suffer from spontaneous fractures, progressive osteomalacia, bone pain and dental abscesses.

Exhibit 5: Dental abscesses due to XLH

Source: NIDCR

Exhibit 6: 'Bow-leggedness' typical of XLH and rickets

Source: 'Rickets radiograph,' Wikimedia Commons

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Current treatments can only 'put a finger in the dyke' of Pi dysregulation. KRN23 on the other hand solves the root of the problem.

Current treatments for XLH

The current standard of care for XLH patients suggested by specialists is a closely monitored therapy of oral inorganic phosphate and/or vitamin D. This regimen may aid bone mineralization by increasing net phosphate intake and intestinal absorption, but has been shown to only transiently increase serum Pi concentrations and requires extremely close monitoring as a result. Unfortunately, many complications of this treatment occur, most often being hypercalciuria (increased urinary calcium), calcification of soft tissues such as the kidneys, tendons and components of the cardiovascular system, and hyperparathyroidism (excessive production of parathyroid hormone [PTH]). These complications highlight the fact that these treatments do not treat the root cause of the disease (e.g. excess FGF23), but rather attempt to overload the broken feedback loop into a more favorable direction. Additionally, compliance is an issue given the requirement for 3-4x daily dosing (especially in pediatric patients) and chalky stools.

Therapies are viewed as being most important for children as it will literally shape their long term development and growth. Treatment in adults is typically used in patients with severe symptoms and/or those who are undergoing orthopedic surgeries, have bone fractures or are in need of corrective dental procedures.

KRN23 Preclinical/Clinical Development

Preclinical

In preclinical studies done by KHK in a mouse model of XLH (Hyp – deleted PHEX gene), a single dose of the FGF23 antibody (4 or 16mg/kg) increased serum phosphate levels to or higher than that found in the wild type mouse while calcium levels were unchanged. At the 16 mg/kg dose, phosphate excretion was reduced to that of the wild type mice and the renal cotransporter expression was restored. KHK also administered 4 weekly injections at 4 or 16 mg/kg to Hyp mice for assessment of improvements in bone morphology. Tail length steadily increased in Hyp mice through 28 days of treatment relative to untreated Hyp mice but did not reach wild type levels at 28 days. Femur/tibia lengths and bone density were also increased.

Phase 1 trial

The phase 1 study for KRN23 was run by KHK and was a double-blind, randomized, placebo-controlled, single dose, dose-escalation study in 38 adults with a clinical diagnosis of XLH. Patients were randomized 3:1 to KRN23 (N=29) or placebo (N=9), with KRN23 patients receiving a single dose either IV (0.003, 0.01, 0.03 0.1 and 0.3 mg/kg; N=17) or SQ (0.1, 0.3, 0.6 and 1.0 mg/kg; N=12). Primary outcomes for the study were safety and tolerability, and secondary outcomes related to pharmacodynamics related to serum Pi and vitamin D. All patients either were not receiving or discontinued vitamin D and/or phosphate supplementation 10 days prior to and until the completion of the study.

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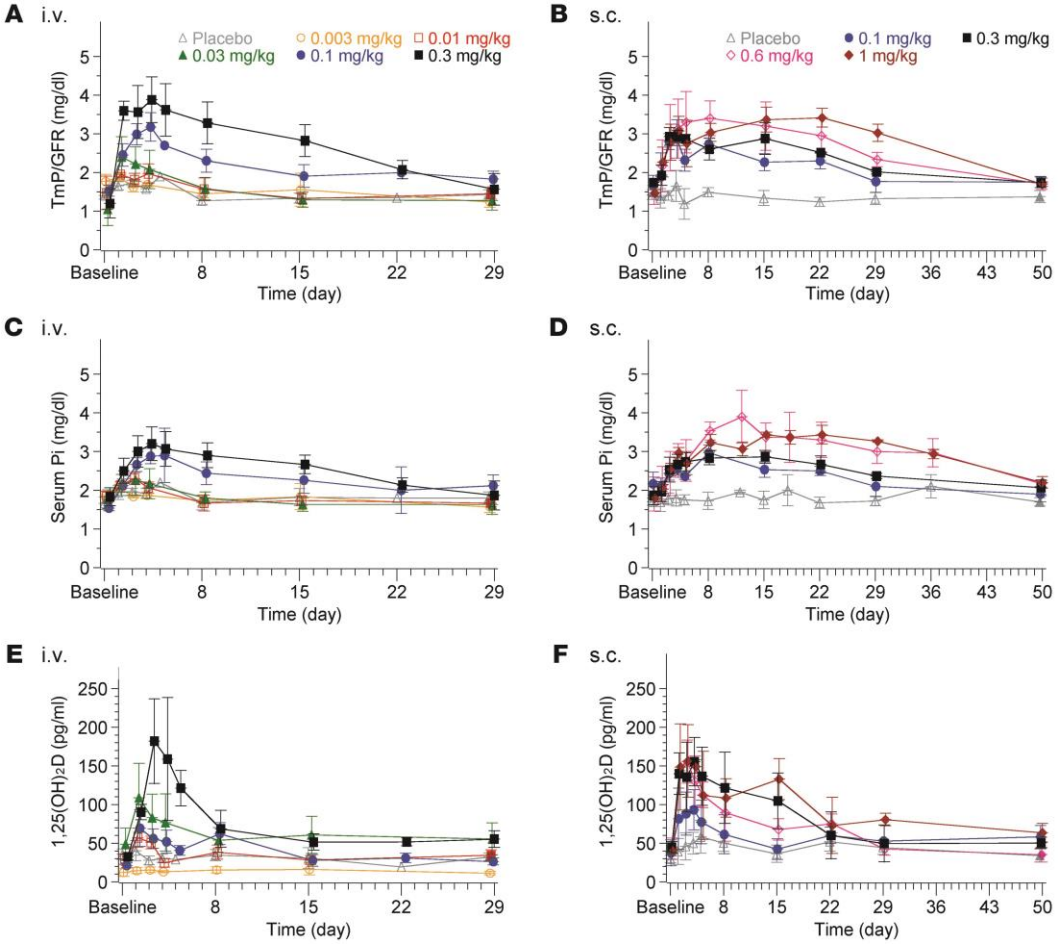
Exhibit 7: PK outcomes of KRN23 administration



Source: Company Data

A single dose of KRN23 increased TmP/GFR, serum Pi, and Vitamin D levels in adults with XLH

Both IV and SQ KRN23 significantly increased serum Pi, renal reabsorption of Pi (TmP/GFR) and transiently increased vitamin D (not very durable after 15 days). SQ administration had an increased time to benefit (8-15 days vs. 0.5-4 days with IV) but a longer duration of action (>29 days post-injection at higher doses) and numerically higher increase in Pi measures over the trial period. This longer lasting effect of the SQ administration was mirrored by sustained higher serum Pi concentrations when compared to IV administration and suggested the possibility for once monthly SQ dosing.

There was a higher frequency of adverse events (AEs) in patients receiving KRN23 treatment (83%) vs. placebo (45%). Six patients were considered to have treatment related AEs: increased blood amylase (2 patients), nausea (2 patients), dizziness, headache and blood pressure increases (6% each). There were no clinical signs of abnormal dysregulation of phosphate metabolism as a result of treatment (e.g. nephrocalcinosis, hypercalciuria, hypercalcemia or hyperthyroidism). Additionally, no MTD was reached, no anti-KRN23 antibodies (key for chronic administration), and no infusion related reactions were noted. PTH levels were numerically (but not statistically significantly) increased with higher doses of KRN23. This increase is likely not of clinical importance given that there were no changes in serum calcium levels (the potential negative consequence of hyperparathyroidism).

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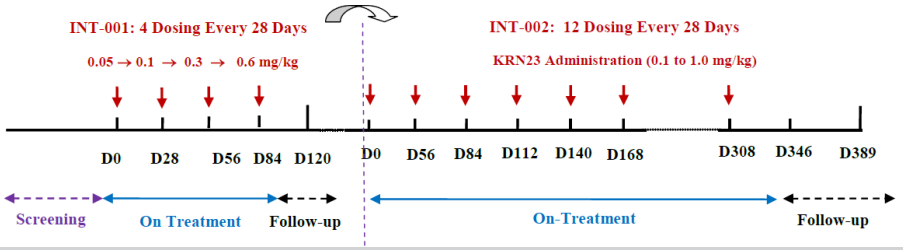
Phase 2 results suggest repeat dosing of UX023 was well tolerated and effective at raising Pi levels.

Phase 1/2 adult repeat dose study with SQ KRN23

A phase 1/2 study evaluating repeated SQ dosing of KRN23 was recently completed, and data was presented at the ICE/ENDO meeting in June. 28 XLH patients were recruited as either an extension of the previous phase 1 study, or new patients. The study was designed as an open-label dose escalation study, where each patient received escalating doses (0.05, 0.1, 0.3 and 0.6 mg/kg) of SQ KRN23 every 28 days, for up to 4 cycles and then followed in an extension study for up to 13.5 months. The dosing in this study was based on serum Pi on day 25/26 after the first dose. The primary efficacy endpoint assessed the proportion of patients with post-dose serum Pi in the ranges (2.5 to ≤ 3.5, 3.5 to ≤ 4.5, and >4.5mg/dL) and secondary endpoints included changes from baseline in TmP/GFR, serum Pi, serum Vit D, and PK/PD. Primary safety endpoints included a composite of immunogenicity, AEs, renal ultrasound, cardiac CT, clinically significant changes in vital signs and laboratory tests. At baseline, ~96% of the patients had serum Pi < 2.5 mg/dL and the mean serum Pi at baseline was 1.9±0.3 mg/dL.

Exhibit 8: KRN23 Phase 1/2 dosing regimen



Source: Company Data

In the dose escalation phase, the mean doses (± SD) administered per cycle were 0.05, 0.10 ± 0.01, 0.28 ± 0.06 and 0.48 ± 0.16 mg/kg, indicating that by the fourth cycle most patients were on the highest 0.6 mg/kg dose. Serum Pi increased in all patients and after the 4th dose peak mean serum Pi was increased to 3.03±0.42 mg/dL (~60% increase over baseline; ~89% of patients reached the low end of the normal range). TMP/GFR was significantly increased following treatment cycles 2 – 4 and vitamin D was increased after treatment cycles 3 and 4. PK data demonstrate that serum Pi peaks 7 days following a dose of KRN23, whereas vitamin D peaks sooner at 3-7 days post-dose. The bone remodeling marker P1NP was significantly increased ($p<0.05$) after all doses and osteocalcin was increased significantly only after the fourth dose. Importantly, while prior KRN23 data had suggested this may be the case, this was the first dataset that established the link between increases in serum Pi and improvements in markers of bone remodeling. Mean scores from baseline on two QoL measures (SF-36v2 and WOMAC) improved after the fourth dose. In SF-36v2, statistically significant increases were observed in the role limitations due to physical health, bodily pain, and physical component summary scales. For WOMAC, statistically significant increases were observed in the physical functioning and stiffness scales (one of the major symptoms in XLH patients). There were no clinically significant changes in parathyroid hormone, serum calcium, or urinary calcium excretion. No patients experienced serum Pi > 4.5 mg/dL which is critical given that the formation of phosphate precipitates requires sustained serum Pi's of 7-8 mg/dL. One patient discontinued KRN23 due to injection site utricaria ('hive-like' symptoms), and the most common AEs were nasopharyngitis (inflammation of the upper respiratory tract), joint pain, diarrhea, back pain, and restless legs syndrome. No anti-KRN23 antibodies, changes in ECG, renal or cardiac tissue calcification or any SAEs related to calcification were observed during this study.

Data from the overall study including the extension portion evaluating an additional 12 doses (total of 16 doses over 16 months) in 22/28 patients were presented recently at the

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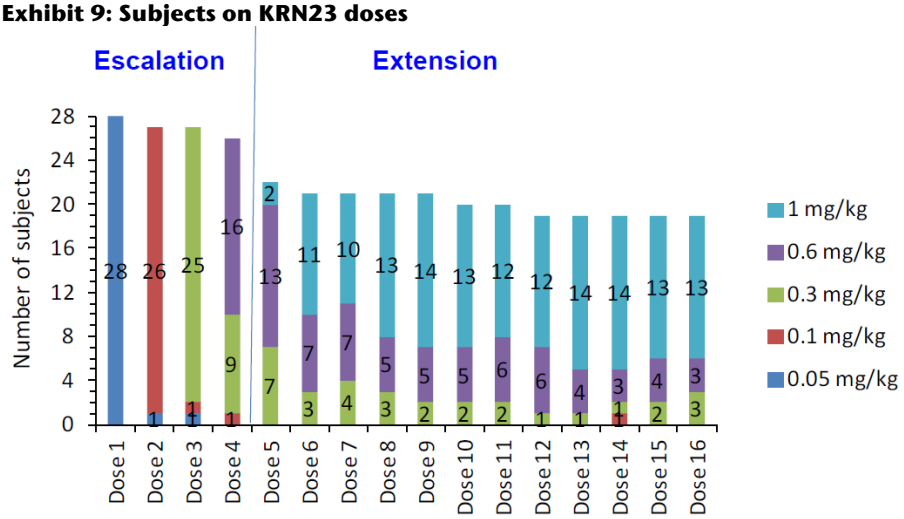
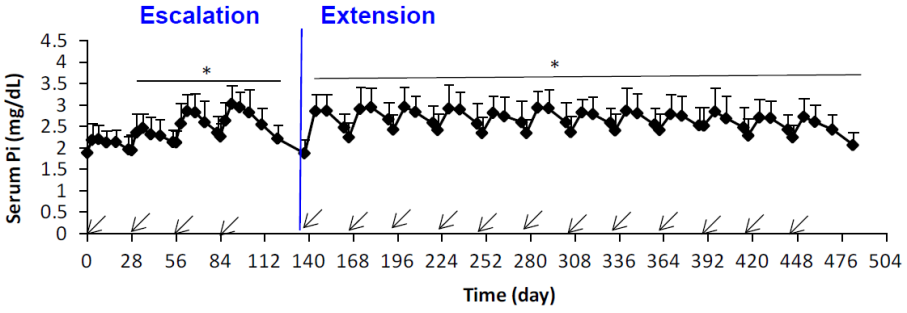
ASBMR meeting. A majority of the patients in the extension phase (13/22) were on the highest dose (1mg/kg) by the end of the study. Increases in serum Pi, serum Vit D, and TmP/GFR were sustained from the escalation portion although Vit D levels tended to decrease over time. Serum Pi of 52.6% - 85.7% of patients in the extension portion reached the normal range of 2.5 – 4.5 mg/Dl at peak time on day 7 or day 14 after each dose. The bone remodeling marker P1NP and osteocalcin sustained the increased levels from month 4.

Exhibit 9: Subjects on KRN23 doses



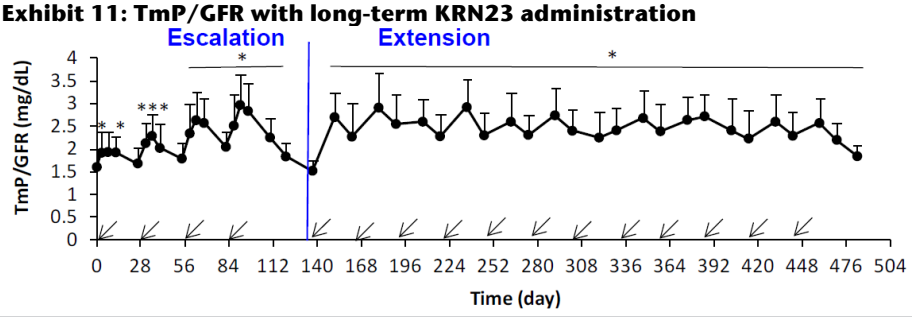
Source: Company Data

Exhibit 10: Serum Pi with long-term KRN23 administration



Source: Company Data

Exhibit 11: TmP/GFR with long-term KRN23 administration



Source: Company Data

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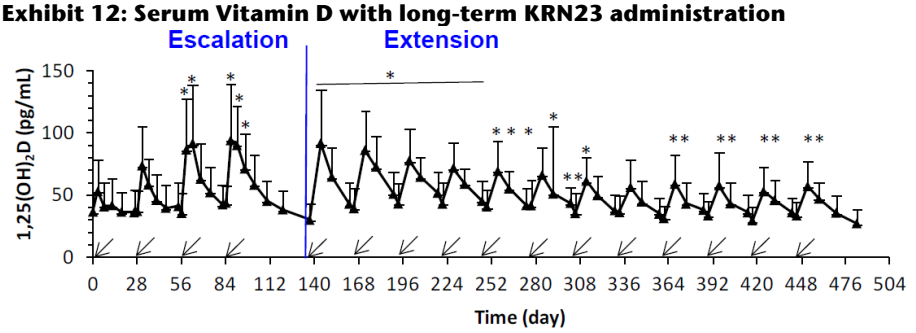
Exhibit 12: Serum Vitamin D with long-term KRN23 administration



Source: Company Data

There were no clinically significant changes in parathyroid hormone with some increases towards the end of the study. Mean serum calcium increased slightly with mild intermittent hypercalcemia in 2 patients and transient increases in urinary calcium was seen in 4 patients. No patients experienced serum Pi > 4.5 mg/dL and no patients developed anti-KRN23 antibodies. Drug related AEs included injection site reactions (n=5), diarrhea and arthralgia (n=3), and 2 patients each with injection site erythema, injection site pain, upper abdominal pain, headache, restless legs syndrome, and decreased neutrophil count. Renal ultrasounds indicated no worsening of nephrocalcinosis in any patient, and cardiac CTs detected a modest increase in coronary artery calcification scores that were considered minimal and not clinically relevant. ECGs also indicated no clinically significant abnormalities in any patients and no left ventricular hypertrophy was observed.

Future development plans for KRN23 – Pediatrics are the key focus

RARE plans to focus on pediatric patients (at least initially) for further development of KRN23. Children with XLH are facing not only a lifetime of negative consequences from hypophosphatemia, but also stand to benefit from early intervention in terms of normal long bone growth. Children's bones also have a high rate of growth and bone formation and may also be the patients with the greatest potential for improvement. RARE recently initiated a phase 2 study in pediatric XLH patients after consultation with the FDA and MHRA in the UK. The study will be a randomized, open label study in 30 prepubertal (ages 5-12) pediatric XLH patients to identify the dose and dosing regimen for a phase 3 study. It will comprise a 16 week dose titration period to identify the individualized KRN23 dose that produces stable serum phosphorus levels in the target range followed by a 48 week treatment period when patients will receive their optimized KRN23 dose on a monthly or biweekly basis. An interim analysis for safety and pharmacodynamic data will be conducted 24 weeks after the titration period at week 40. Additionally, the study will evaluate preliminary clinical effects of KRN23 treatment on bone health and deformity as measured by blinded radiographic assessments, growth, and muscle strength, and motor function will also be assessed. Additionally, KRN23's impact on markers of bone health and patient-reported outcomes of pain, disability, and quality of life will be evaluated.

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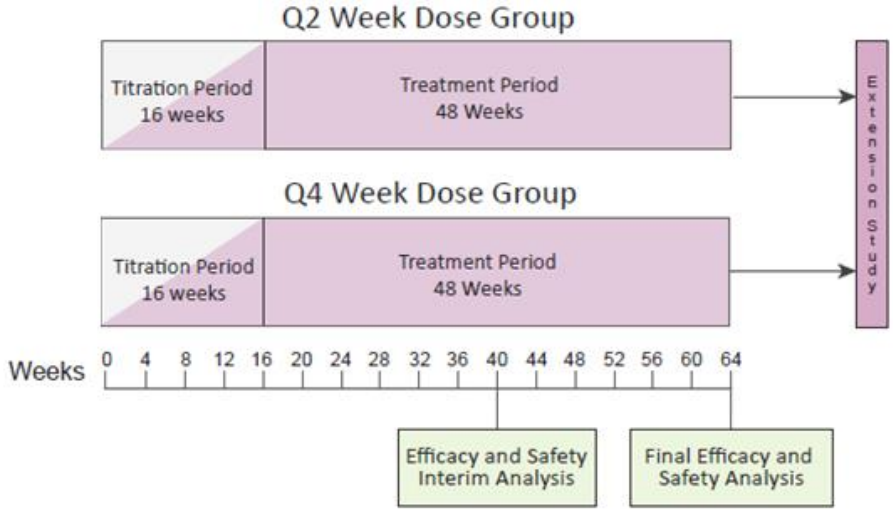
Exhibit 13: Phase 2 trial design for KRN23 in pediatric patients



Source: Company Data

If the phase 2 trial is successful, RARE plans to initiate a pivotal phase 3 trial in pediatric patients. This could happen as early as 2H15 depending on the interim data. Recently, management disclosed some of the feedback received from the FDA on the design of the phase 3 study. These included: 1) the potential for the study to be open label but FDA recommended inclusion of a standard of care control arm for non-inferiority comparisons, and 2) primary endpoint measures comprising blinded radiographic assessments of changes in bone abnormalities like rickets and bowing, and changes in growth. RARE plans to finalize the phase 3 study design in pediatric patients after consulting with the FDA further and obtaining additional safety and efficacy data. Although children will be the focus, a parallel phase 2b study in adults is also planned.

Competitive landscape

As far as we can tell there are no other commercial interests in developing a therapy for XLH. Despite this, there are two other early stage clinical trials investigating therapies. In one study sponsored by Yale University, nasal calcitonin (aka thyroid hormone), a putative suppressor of FGF23 production, is administered and then both FGF23 and serum Pi will be measured. Although the investigators have some preclinical data to support calcitonin as an FGF23 suppressor, we do not view this approach as equal or superior to KRN23 as: 1) the mechanism by which calcitonin suppresses FGF23 action is unknown, and 2) calcitonin's primary function is to reduce circulating calcium levels. We predict that although this approach may ultimately be effective in reducing FGF23 signaling, it will likely complicate treatment due to calcitonin's effects on calcium homeostasis.

In another study, which is sponsored by the NIH, patients will be given cinacalcet (a.k.a. Amgen's Sensipar) in conjunction with standard of care treatment of dietary phosphate and vitamin D. We view this approach as vastly inferior, in that it relies on current standard of care, and ultimately can only improve the pharmacodynamics associated with these treatments and does not solve the root of the problem: overproduction of FGF23.

Two drugs have been evaluated preclinically by academic labs where they have demonstrated normalization of serum Pi in the Hyp mouse model of XLH but they have not been moved into the clinic. Hexa-D-arginine (D6R) inhibits FGF23 by activating subtilisin like protein convertase-2 (SPC2) and C-terminal FGF23 competes with FGF23 thereby reducing its activity.

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Gene therapy is a possible approach but we are not aware of any being pursued for XLH. Since the current standard of care of phosphate and vitamin D is relatively inexpensive, it is quite possible that patients in some countries may not use KRN23.

XLH Market Opportunity

We estimate that KRN23 is launched globally in 2018 at an annualized price of $85,000/patient with patent expiration in 2029. We assume that the prevalent XLH population in the US and EU totals ~36,000 XLH patients, of which 25% are pediatric patients; in LATAM, we assume a prevalence rate of 3.8/100K, with the same relative proportion of pediatric patients. In the US and EU, we assume KRN23 peak penetration of 18% and 70% in adult and pediatric patients, respectively; in LATAM, we assume KRN23 peak penetration of 3% and 20% in adult and pediatric patients, respectively. We have assumed RARE receives a royalty of 27% (first 5 years of profit share approximate this royalty rate) in the US and 10% in the EU resulting in peak adjusted royalties of $125M and $50M, respectively, in these regions. RARE will pay out a 2% royalty on LATAM sales to KHK where we forecast peak adjusted sales of $122M. Combining royalties from both the US and EU with the net sales from LATAM, we project WW adjusted revenues to RARE of ~$295M.

Triheptanoin – a versatile energy source for the treatment of LC-FAOD and GLUT1 deficiency

Triheptanoin (THN) is a purified form of a unique medium length odd chain fatty acid triglyceride constructed of a 'glycerol backbone' and 3 moieties of the 7 carbon fatty acid (FA) heptanoate. THN was in-licensed from Baylor University to whom RARE will owe a mid-single digit royalty. A great deal of basic work was done at Baylor characterizing the metabolism of heptanoate generally, and specifically in treating the metabolic disorder Long-Chain Fatty Acid Oxidation Disorders (LC-FAOD). LC-FAODs are a set of autosomal recessive metabolic disorders characterized by a mitochondrial enzyme deficiency due to which LC FAs are not metabolized into acetyl-coenzyme A that is then converted into energy via the Kreb's/TCA cycle. This leads to a shortage of energy during exercise, fasting, and illness with symptoms of low blood sugar (hypoglycemia), muscle rupture (rhabdomyolosis), and heart/liver disease and is also known to be a cause of sudden infant death syndrome (SIDS). Heptanoate is a versatile energy source for all tissues in our body due to two important structural features: 1) it easily crosses membranes due to its size (a medium chain FA, meaning 6-12 carbons in length), and 2) it can be converted to various essential molecules that tissues require to perform their intended functions. RARE has estimated a prevalence of 2,000-3,500 LC-FAOD patients in the US and has identified 1,300 patients globally with > 600 of these patients in the US. THN is currently in a phase 2 study in severe LC-FAOD patients with interim data expected in 2H15. Recently, RARE had a US patent granted with claims to THN above a certain level of purity that is set to expire in October 2025. We estimate THN will be launched for LC-FAOD in 2018 generating peak adjusted worldwide sales of $328M

THN - an alternate energy source to LC fat

Tissues in our bodies have a 'preferred' energy source. THN is a perfect 'second choice' when something metabolically goes wrong.

All macronutrients (proteins, carbohydrates and fats) that we consume or produce can be metabolized to some degree throughout our bodies, but each tissue has a 'preference' for a particular nutrient or a ratio amongst certain components. For example, neuronal tissue

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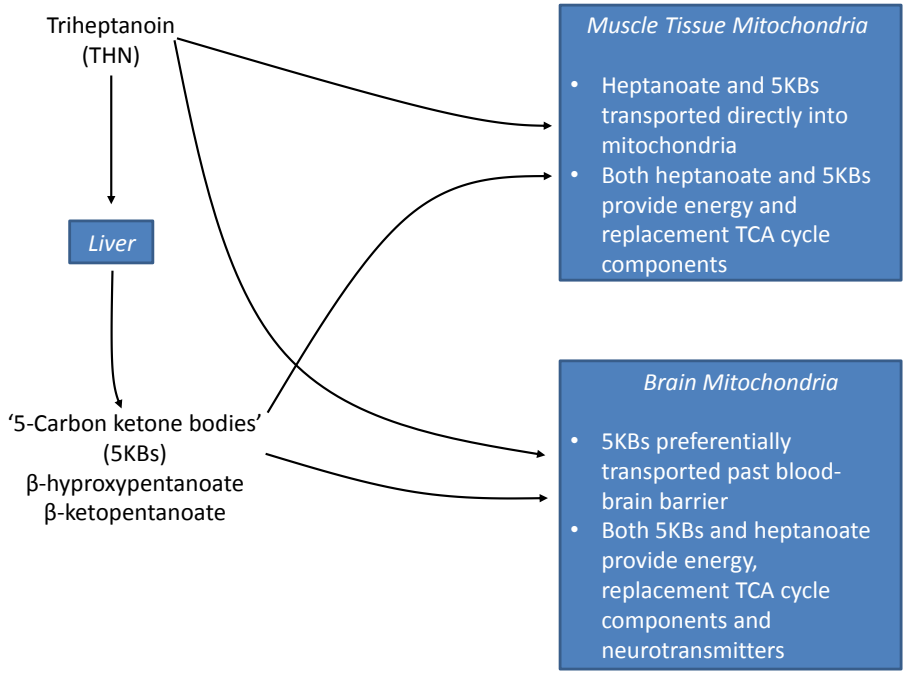
preferentially metabolizes glucose (a carbohydrate) whereas muscle tissue utilizes fats at a higher rate. These local preferences are dictated both by the 'equipment' these cells have to breakdown (or catabolize) these nutrients, but also their specific needs for energy and the necessary building-blocks to create specialized molecules (e.g. neurotransmitters in the brain). In cases of metabolic disorders, these preferred energy sources may not be available to the tissues either because they cannot transport the nutrient inside the cells (i.e. a transporter malfunction) or once inside the cell the nutrient cannot be properly processed (i.e. an enzymatic malfunction). THN is the perfect 'second-choice' for tissues that have certain malfunctions in their nutrient processing system.

THN uniquely provides the optimal ratio of A-CoA:P-CoA (2:1) required for the perpetuation of the TCA/Kreb's cycle.

Upon entering the bloodstream, THN is taken up by most tissues because it can be passively diffused across membranes without requiring any specialized transporters. THN may then enter the mitochondria, or the 'power plants' of a cell, where it is catabolized into two components: 1) acetyl-CoA (A-CoA) which can be used to produce energy, and 2) propionyl-CoA (P-CoA) which can be used either for energy or as a building block for essential molecules. While both A-CoA and P-CoA can be derived from other sources, the 'goldilocks' or optimal ratio of 2 A-CoA: 1P-CoA which is provided by THN is truly unique. This 2:1 ratio allows for the perpetuation of the citrate acid cycle (TCA, aka tricarboxylic cycle or the Krebs cycle), or the series of chemical reactions within the mitochondria that provides the majority of our cellular energy, thus remedying any deficiencies in energy during metabolic disorders. Finally, THN may also be converted into the 5-carbon ketone bodies (5KBs) β-hydroxypentanoate and β-ketopentnoate in the liver. The 5KBs can either be converted into glucose directly or used as an alternative energy source. These 5KBs provide the same 2:1 ratio of A-CoA and P-CoA when catabolized, but are more easily transported into neuronal tissue.

Exhibit 14: THN metabolism



Source: Jefferies

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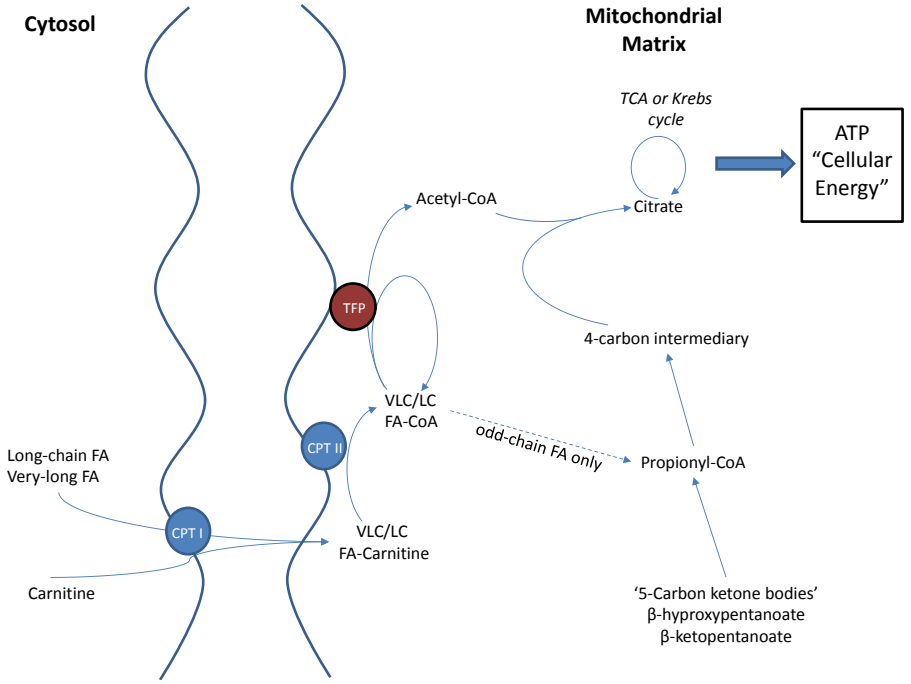
LC-FAOD

Long-Chain and Very long-Chain Fatty acid oxidation

Long-chain (LC; 13-21 carbons in length) and very-long-chain (VLC; > 22 carbons in length) fatty acids are relatively large molecules, and as such require some specialized enzymes for their oxidation (e.g. 'break-down' or catabolism). Like all other FAs, LC and VLC-FAs are oxidized in the mitochondria in a process called β-oxidation, but unlike shorter FAs these must be transported into the mitochondria using carnitine palmyltransferase I & II (CPT I & II). Once inside the mitochondrial matrix, the LC and VLC FAs are progressively catabolized into A-CoA and P-CoA by a specialized group of enzymes: tri-functional protein (TFP, an enzymatic complex that breaks down FAs), long-chain acyl-CoA dehydrogenase (LCAD), and very-long-chain acyl-CoA dehydrogenase (VLCAD). FAs with an even number of carbons are completely broken down into A-CoA, whereas FAs with an odd number of carbons also produce one P-CoA. While both A-CoA and P-CoA enter the TCA/Kreb's cycle, P-CoA is very important in maintaining the balance of the cycle by providing a source of intermediate components which can become depleted by use in other biosynthetic pathways (e.g. gluconeogenesis or amino acid synthesis). As an end result, β-oxidation and the TCA results in a great deal of ATP, the major cellular currency used throughout the body.

Exhibit 15: LC and VLC FA metabolism



Source: Jefferies

LC and VLC-FAOD: breakdown in key limiting steps of β-oxidation and the TCA

LC and VLC-FAOD diseases are caused by deficiencies in CPT II (the enzyme that allows transportation of LC and VLC-FAs into the mitochondria), TFP, LCAD and/or VLCAD (the enzymes responsible for breaking down larger FAs into smaller sub-units). Irrespective of the specific genetic disruption, the net result of failed utilization of these FAs is three-fold: **1)** an intracellular build-up of harmful levels of LC and VLC-FA derivatives (potentially with carnitine depletion if CPT II deficiency); **2)** rapid depletion of glucose (hypoglycemia) in an attempt to maintain energy demands; and **3)** an overall drastic

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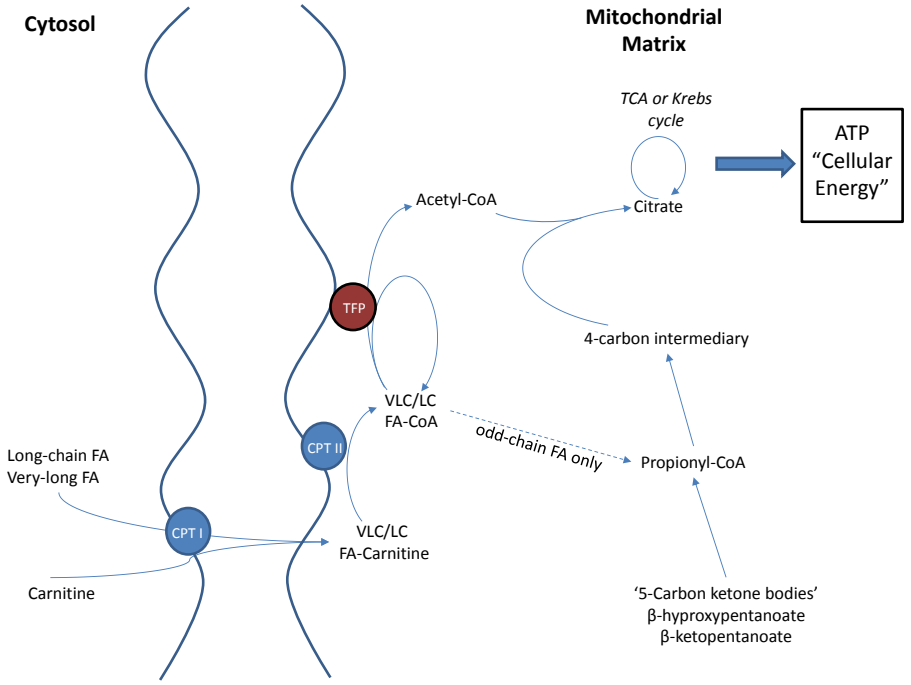
reduction of available ATP in tissues. Because muscle tissue (both skeletal and cardiac) preferentially uses fats as energy sources, it is disproportionately affected by the negative consequences of these disorders.

Exhibit 16: Biochemical consequences of LC/VLC-FAOD



Source: Jefferies

LC and VLC-FAOD symptoms and diagnosis

Clinically, these disorders can range in severity from no symptoms (rarely) to increasingly severe manifestations, including hypotonia (muscle weakness), acute and chronic cardiomyopathy (heart uses LC FAs for >50% of its energy), intermittent rhabdomyolysis (rupture of muscle fibers), hypoglycemia, peripheral neuropathy and even sudden death. Symptoms are often worse between meals, during illness, or exercise. Some patients are frequently hospitalized due to these symptoms. Onset of these disorders can be very early (often leading to fetal/infant mortality) or delayed until adulthood. Given the wide range of symptomology and age of onset, these metabolic disorders have proven to be difficult to diagnose, with only *in vitro* assays of FA metabolism within a patient's cultured cells having proven to be consistently accurate. Genetic screenings have also been used as a potential diagnostic; however, geneticists warn that not all disruptive mutations for these disorders have been identified. Due to the potential for newborn fatalities associated with severe FAODs, this class of disorders has been included in the sudden infant death syndrome (SIDS) newborn screening. In regions where newborn screening does not exist, many patients are identified after being hospitalized due to a hypoglycemic event where the patient does not have any ketones (typically indicating a blockage not within the Kreb's cycle that would have resulted in excess Acetyl-CoA and ketone bodies).

Current treatments for LC and VLC-FAOD

Current treatments for LC/VLC FAODs all include a careful control of both diet and behavior, with the common goals of avoiding lipid mobilization and their failed oxidation. Behaviorally, all patients with these FAODs are advised to avoid fasting (a state which causes lipid mobilization from adipose tissue), and patients with muscle weakness must

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also avoid strenuous activities. Dietary treatments include the restriction of dietary fat, regular high-carbohydrate meals (sometimes supplemented with insulin), supplementation of medium-chain triglycerides (MCTs) and/or carnitine (amino acid derivative that plays a key role in energy production). MCT oil comprises medium chain fatty acids derived from plant extracts like palm and coconut oil that are oxidized by medium chain fatty acid enzymes thus avoiding the long-chain defective ones. MCT oil is not as effective as THN as it does not provide odd chain fatty acid intermediary molecules for the Kreb's cycle and cannot be converted into glucose. MCT oil has been known to have poor GI tolerability that is somewhat improved when mixed with food but compliance is also impacted by impurities that produce an unpleasant smell and taste. MCT oil based diets cost patients ~$10-$15,000 per year. B. Braun Medical has received orphan drug designation for THN in Europe but has not initiated any clinical development. While other medium odd chain fatty acids or gene therapy approaches could be pursued, we are not aware of any being pursued at this time.

When used in concert, current treatments can prevent the most severe symptoms (potentially deadly cardiomyopathies and rhabdomyolysis), but do not seem to improve the constant cellular energy deficiency characteristic of these disorders. Additionally, these measures require constant monitoring as any lapse in care could lead to serious deleterious consequences.

THN Clinical Development for LC-FAOD

Historical Triheptanoin treatment for FAODs

Unlike other treatments, such as MCT oil, THN treatment offers a solution to both major problems in LC-FAODs. First, due to its size, heptanoate is transported into the mitochondria without the CPT I/II system. Secondly, the 'odd-carbon' FA heptanoate also provides substrate for the necessary TCA cycle intermediary molecules that can become depleted by various biological pathways.

Since THN was first developed at Baylor Research Institute a number of patients (~130) have been treated in investigator sponsored trials for over a decade of which 65 had LC-FAODs. Treatment emergent AEs included GI side effects and weight gain that could be managed by titrating the dose at therapy initiation and managing caloric intake. SAEs consistent with the underlying disease included muscle weakness/pain, myoglobinuria (muscle protein in urine), muscle cell rupture, metabolic crisis, cardiomyopathy, hypoglycemia, and elevated CK. Other SAEs included respiratory distress/breathing problems, failing oxygen saturation rate, seizure, infections, fever and vomiting from unspecified cause, and medical procedures. Three SAEs were considered possibly related to THN - muscle cell rupture and elevated CK in 2 patients and myoblobinuria that was seen in 1 patient in conjunction with exercise, suboptimal THN dose, and no fluid intake. Six of these patients died but none were considered related to THN use.

Prior to any placebo-controlled randomized trials, THN was administered to 48 patients suffering from various LC-FAODs due to a variety of mutations (CPT-I, CPT-II, CACT, VLCAD, LCHAD, TFP, and SCAD) and data was reported on changes in reported symptoms on standard of care and THN by Baylor University in 2006. In general, it appears that the THN treatment greatly improved the most serious conditions, including cardiomyopathies, hypoglycemia, hepatomegaly, rhabdomyolosis, and weakness/fatigue although there was no change in retinopathy. THN treatment also had a favorable mortality profile when comparing it to another study that evaluated standard of care therapy suggesting potential for THN to drive a survival benefit (21 of 41 or 51% MCT patients died vs. 3 of 48 or 6% THN patients died).

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Exhibit 17: Retrospective meta-analysis of THN treatment in LC-FAODs

	# of symptomatic patients	
Symptoms	Before THN (MCT and/or low-fat, high-carb)	Post THN
Cardiac	10	1
Rhabdomyolysis	36	15
Weakness/fatigue	44	10
Hypoglycemia	24	1
Hepatomegaly	26	2
Retinopathy	3	3
Total	**143**	**32**

Source: Company Data

A retrospective analysis (pre and post-THN) of charts from 20 patients suffering from the most severe cases of FAODs treated with THN for up to 13 years done by the Univ. of Pittsburg suggests similar findings. All measures reported were reduced by THN treatment in these patients, but hospital days/year (69% reduction) and hypoglycemia events/year (96% reduction) were significantly reduced. The number of hospitalizations was also reduced by 36%. It should be noted, that THN treatment was well tolerated, and in one case a patient continued to receive the treatment for 13 years. Despite the overall tolerability and efficacy suggested by the historical data, THN had a relatively lower efficacy for reducing rhabdomyolysis although mean peak creatine kinase (measure of the extent of muscle destruction) during rhabdomyolosis was reduced by 68%. There was no effect on peripheral neuropathies and retinopathies. These data suggest that in the most severe patients THN may be able to resolve some of the symptoms of the disease.

Exhibit 18: Retrospective analysis of compassionate use THN patients

Description	Pre-THN	Post-THN	% Decrease	n	p-value
Mean hospital days/year	17.55	5.4	69%	15	**0.0242**
Mean total hospitalizations/year	1.94	1.26	36%	16	0.1126
Mean infant total hospitalizations/year	13.01	1.37	89%	4	0.0892
Mean hypoglycemia total hospital days/year	8.42	0.18	98%	9	**0.0257**
Mean hypoglycemia events/year	0.92	0.04	96%	9	**0.0091**
Mean rhabdomyolysis total hospital days/year	5.94	2.16	64%	9	0.1224
Mean rhabdomyolysis events/year	1.05	0.68	35%	11	0.4604
Mean peak creatine kinase for rhabdomyolysis events	85,855	25,797	68%	7	0.1279

Source: Company Data

Ongoing Phase 2 trial

RARE is currently enrolling ~30 patients (6 months – 35 years) with severe LC-FAODs (CPT-II, VLCAD, TFP, or LCHAD; CACT or CPT-I are excluded) into an open-label Phase 2 trial at 8 sites in the US and Europe. All patients enrolled will be currently managed with MCT oil and/or a low-fat and high-carb diet, but having clinical manifestations associated with LC-FAODs. These clinical manifestations despite therapy could include any one of: chronic elevated CK levels and at least 2 or 4 major clinical events in the past 1 or 2 years respectively; episodic elevated CK levels with reported muscle dysfunction; highly elevated CK but asymptomatic; ER/acute care visits or hospitalizations for hypoglycemia, rhabdomyolosis, or exacerbation of cardiomyopathy (≥ 3 in 1 year or 5 in 2 years); severe susceptibility to hypoglycemia after short periods of fasting or recurrent symptomatic hypoglycemia; and functional cardiomyopathy requiring ongoing medical management.

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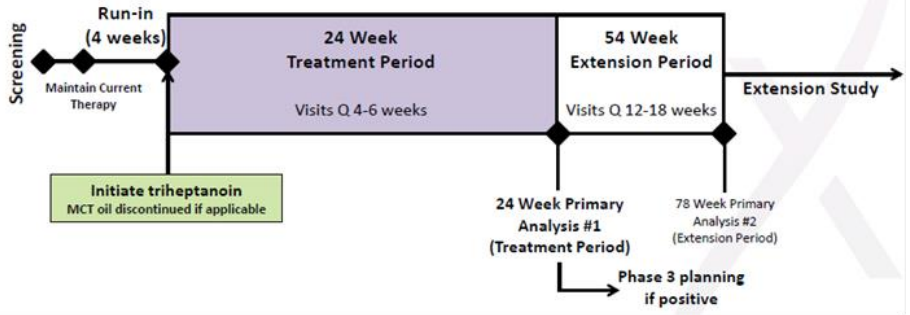
After a 4 week baseline run-in period on standard treatment, patients will receive THN at ~25-35% of total daily caloric intake spread across at least 4 administrations per day for 24 weeks. Patients can continue to be dosed for an additional 54 week period. The primary endpoint will evaluate the change from baseline over 24 weeks with THN treatment in 3 key areas associated with these disorders: 1) skeletal myopathy (e.g. rhabdomyolysis, muscle weakness, exercise test); 2) hepatic disease (e.g. hypoglycemia and hepatomegaly); and 3) cardiac disease (cardiomyopathy events, ECG measures). Secondary measures include composite safety scores of AEs and overall energy metabolism measures. The overall goal for this study is to determine appropriate endpoints for a phase 3 trial, and to optimize inclusion criteria. Interim data at the end of the 24 week treatment period from this study is expected in Mid-15. RARE is also supporting multiple compassionate use programs and ISTs with THN in LC-FAOD and other indications.

Exhibit 19: Phase 2 trial design for THN in LC-FAOD



Source: Company Data

Competitive landscape

To date there are no other commercial interests in developing specific therapies for the treatment of LC-FAODs. There has been some interest in determining the efficacy of Bezafibrate (a fibrate used to treat hyperlipidemia) in treating LC-FAOD. There were promising early anecdotal and *in vitro* data which suggested that it may be effective in reducing potentially harmful LC acyl-CoA or LC acyl-carnitine molecules, but these findings were not confirmed in a later placebo controlled trial. Specifically, there were no improvements in either fatty acid oxidation or heart rate during exercise, which were the primary efficacy endpoints of the study.

As mentioned earlier, B. Braun Medical has received orphan drug designation for THN in Europe but has not initiated any clinical development. We view THN as superior to the current standard of care, MCT oil, for two main reasons: 1) the consistency of the 7 carbon heptanoate FA ensures carnitine independent transport into the mitochondria; and 2) each odd-carbon chain heptanoate will provide replacement intermediaries for the citrate cycle, improving the likelihood of maintaining appropriate energy production. In contrast, MCT oil is a heterogeneous composition of fatty-acids, and therefore cannot ensure steady carnitine free transport into the mitochondria or a constant supply of TCA intermediary replacement.

LC-FAOD Market Opportunity

We assume that THN is launched globally in 2018 at an annualized price of $85,000/patient with patent expiration in 2025. We assume that the prevalent population

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in the US and EU totals ~8,000 LC-FAOD patients and ROW we assume a prevalence rate of 0.8/100K. We assume peak penetration of 60%, 40% and 15% in the US, EU and ROW, respectively, resulting in peak unadjusted sales of ~$226M, ~$188M and ~$85M in the respective regions. After assuming a 70% probability of success and a 5% royalty rate to Baylor University, THN can achieve peak WW adjusted sales of ~$328M.

Glucose transporter 1 deficiency syndrome (GLUT1 DS)

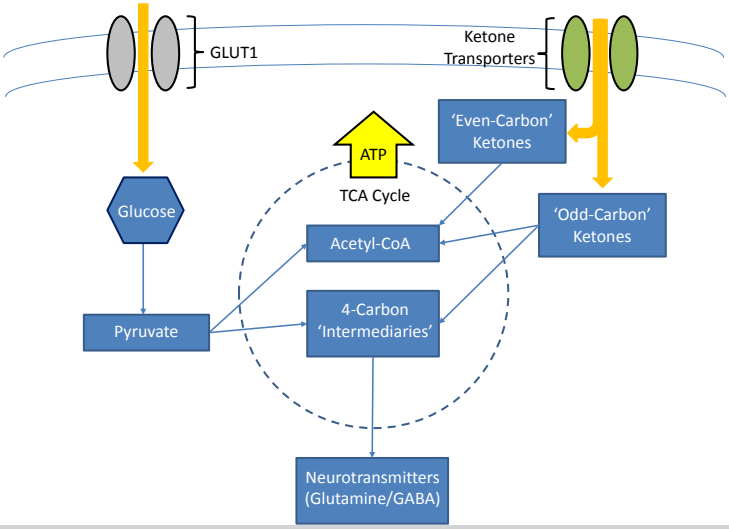
GLUT1 DS patients lack the GLUT1 transporter that enables glucose to cross the blood brain barrier. Mutations in the SLC2A1 gene cause GLUT1 expression to be reduced and/or transport efficiency to be compromised. THN's metabolites (heptanoate and 5KBs) are able to cross this barrier and provide the brain with an alternate energy source. RARE has estimated a prevalence of ~3,000-7,000 patients in the US and has identified >80 patients in the US and >200 globally. THN is currently in a phase 2 study in GLUT1 DS patients who have failed the ketogenic diet and continue to have breakthrough seizures with interim 24 week data expected in Mid-15. Recently, RARE licensed patents to the treatment of refractory epilepsy and other seizure-related and neurologic disorders with THN from UniQuest Pty Ltd. We estimate THN will be launched for GLUT1 DS in 2018 generating peak adjusted worldwide sales of $363M.

Neuronal metabolism and glucose transport

Glucose provides brain tissue with the majority of its energy and substrate to produce neurotransmitters.

The majority of all energy used in the brain is from glucose. In fact, the steady–state normal brain uses approximately 25% of all serum glucose, despite constituting only 1% of total bodyweight. Catabolism of this glucose can enter the TCA cycle as both A-CoA or as pyruvate (a 3-carbon subunit similar to P-CoA). Both of these catabolites ultimately contribute to ATP production (i.e. provide cellular energy), but just like P-CoA pyruvate can also be converted to important TCA intermediary components. These intermediary components are very important to maintain TCA cycle balance (as highlighted in FAODs above), but are also important raw components for the production of neurotransmitters (chief of which are glutamate and GABA).

Exhibit 20: Glucose and Ketone metabolism in the brain



Source: Jefferies

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GLUT1 Deficiency Syndrome

GLUT1 is the only transporter that shuttles glucose across the blood-brain barrier. Patients suffering from GLUT1 DS have a loss-of-function mutation in the gene that codes for this transporter, and therefore have a severely impaired ability to provide the brain with its preferred energy substrate. The primary symptoms of GLUT1 DS are seizures (often those refractory to antiepileptic drugs), episodic movements, acquired microcephaly, neuronal hyperexcitability and delayed and/or impaired brain maturation. Seizures, the most visible symptom, typically onset before the end of the first year of life, and persist through the rest of the patient's life. Current estimates place the prevalence of GLUT1 DS in the US to be 3,000 to 7,000. Diagnosis of GLUT1 DS is based upon the presence of hypoglycorrhacia (low cerebrospinal fluid glucose) with normoglycemia (normal plasma levels of glucose), and then confirmed with a genetic screen. GLUT1 is also the major glucose transporter in red blood cells (RBCs), and as such Columbia University has developed a diagnostic in vitro test using a patient's RBCs. Currently, this diagnostic test is only available for research purposes, but RARE is working with the university to scale up production to clinical/diagnostic scale.

Current treatments of GLUT1 DS

The standard of care for GLUT1 DS is to put the patient on a strict ketogenic diet (KD), which consists of 70-80% of the calories coming from fat and < 10% coming from carbohydrates. In a retrospective study, KD eliminated seizures in approximately 67% (41/61) of GLUT1 DS patients, and of the successfully treated patients ~75% had their seizures cease within 1 month of KD initiation. In addition to KD, antiepileptic drugs (e.g. valparoate and phenobarbital) may also be prescribed to treat seizures, although they have historically had very limited efficacy for this patient population. Children may be on an antiepileptic drug for up to 5 years, but once a GLUT1 DS definitive diagnosis has been made, patients generally switch to KD. Despite the effectiveness of KD in preventing seizures and movement disorders, it does not impact cognitive function and compliance to the diet is difficult due to palatability of the large quantities of fat and the preponderance of enticing carbohydrates currently available. Compliance is made even more difficult in families with multiple children as high-carbohydrate foods are typically easier to obtain in those environments.

Both clinical and preclinical data suggest that the root cause of the CNS dysregulations associated with GLUT1 DS is due to a decline in energy production and a decreased ability to produce adequate levels of neurotransmitters. KD solves the neuronal energy deficit by supplying the brain with an alternative energy source to glucose, ketone bodies. These ketone bodies are produced in the liver from dietary fats, and are then transported past the blood-brain barrier using a transporter system other than GLUT1. Once inside the brain, these ketone bodies may be used for energy substrate, and in the special case of 'odd-chained' ketone bodies, they may also be used as substrates for both TCA cycle intermediaries and perhaps more importantly neurotransmitters.

KD undoubtedly has a high degree of efficacy in treating seizures associated with GLUT1 DS, but it seems to have minimal effect on the other neurological symptoms (e.g. impaired cognition and brain maturation). It is hypothesized that KD is ineffective in treating the non-seizure symptoms because it offers a low level of 'odd-chain' ketone bodies, and therefore a lower level of TCA intermediaries and neurotransmitters. THN treatment will theoretically solve both of the problems caused by GLUT1 DS through its conversion to the 5KBs in the liver. The overall volume of 5KBs produced will provide sufficient energy, and the optimal 2:1 ratio of A-CoA to P-CoA/pyruvate will allow perpetuation of the TCA cycle and adequate neurotransmitter biosynthesis.

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Gene therapy approaches are being pursued but are still early and do not pose a significant threat to THN.

THN Clinical data in GLUT1 DS

Dr. Juan Pascual at UT Southwestern recently published results from an IST with THN in 14 GLUT1 DS patients. Neuropsychological testing (PPVT-4) showed an improvement in receptive vocabulary in 7/8 patients and worsening in 1 patient at 3 months of follow up. Five out of eight patients improved with EVT-2 and 2 patients worsened. All patients showed improvement (not significant) on some aspect of neuropsychological testing between baseline and 1 hour after THN. All patients had a reduction in EEG spike wave seizure rates before and after THN at baseline. This was supported by 11/14 patients continuing on the study at 3 months and 10/14 patients at 6 months. There were no SAEs but 1 patient discontinued after 3 weeks due to GI discomfort. Another patient experienced significant weight gain after 2 months (10%) but did not discontinue. Two patients who experienced diarrhea and/or digestive discomfort within days of receiving THN had their symptoms resolve after reducing the dose by 50%.

Phase 2 trial

In March 2014, RARE initiated a phase 2 placebo-controlled trial evaluating the safety and efficacy of THN in ~30 GLUT1 DS patients (1-35 years old) with a confirmed GLUT1 DS diagnosis (by SLC2A mutation). These patients will either not be on or not be fully compliant with a ketogenic diet or other high fat diet but may be on 1-3 antiepileptic drugs during the study. Enrolled patients are also required to have experienced an average of 5 observable seizures per month over the past 6 months. After enrollment, patients will undergo a 6 week evaluation period to obtain baselines during which they must experience at least 4 observable seizures per month with no 3 week seizure free period. Active treatment will be ~35% of caloric intake from THN split across 4 doses with normal meals. The primary endpoint will be the reduction from baseline in the frequency of generalized or partial onset seizures between week 2 and week 8 of treatment. Additionally, safety will be evaluated via AE rates, labs, and ECGs. The secondary outcomes for the study include more specific measures of cognitive functioning and movement. An unblinded interim analysis will be done by the IDMC when ~16 patients complete the double blind treatment period. If the criteria are met at the interim analysis, the sample size will be re-estimated based on the observed treatment difference and standard deviation, for a total of 40-100 patients and will potentially be a registrational study. If interim criteria are not met, the study will continue as a phase 2 study with 40 patients. Following the placebo-controlled treatment period, patients will have the option to continue on THN treatment as part of an open-label extension study for an additional 44 weeks.

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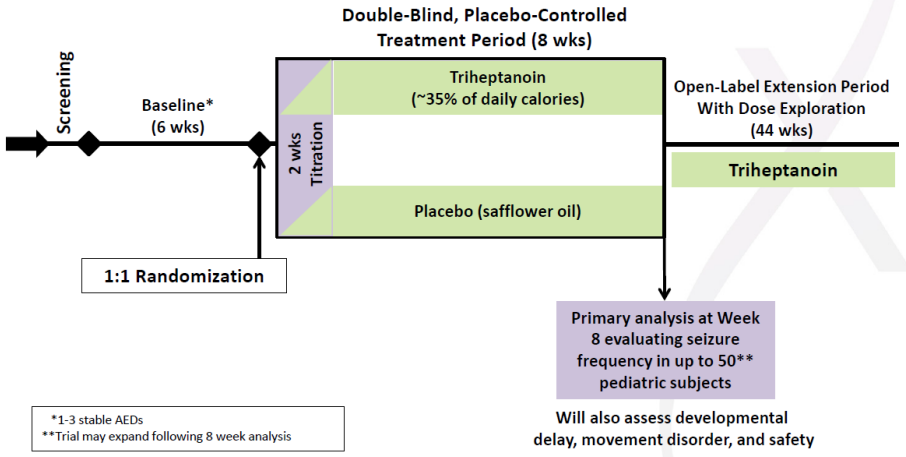
Exhibit 21: Phase 2 trial design of THN treatment for GLUT1 DS



Source: Company Data

Competitive landscape

To our knowledge there are no other commercial interests in developing a treatment for GLUT1 DS. There is however a branded prescription diet, Axona (Accera), currently marketed for the treatment of cognitive decline associated with Alzheimer's disease. Axona is a proprietary MCT blend, with the majority of the FAs as the 8-carbon octanoic acid. We do not view Axona as differentiated from other MCT treatments, as it does not provide the odd chained ketone bodies necessary for replenishment of the TCA cycle or substrate for neurotransmitter biosynthesis.

Glut1 DS Market Opportunity

We assume that THN is launched globally in 2018 at an annualized price of $85,000/patient. We assume that the prevalent population in the US and EU totals ~12,500 GLUT1 DS patients and ROW we assume a prevalence rate of 1.3/100K. We assume peak penetration of 40%, 40% and 15% in the US, EU and ROW, respectively, with peak unadjusted sales of ~$226M, ~$284M and ~$137M in the respective regions. After assuming a 60% probability of success and a 5% royalty rate to Baylor University, THN can achieve peak WW adjusted sales of ~$363M.

Other opportunities for THN

Due to the versatile nature of THN, we view several other potential orphan/ultra-orphan indications related to energy metabolism that may be targetable with THN. Most notably, genetic defects in pyruvate metabolism (both pyruvate dehydrogenase deficiency [PDHD] and pyruvate carboxylase deficiency [PCD]; exact prevalence unknown but estimates of cumulative WW populations at ~4,000-10,000) are devastating and often fatal childhood diseases that result in an inability to convert glucose into an appropriate energy source for the brain. THN could solve this deficiency much in the same way that it does for GLUT1 patients. Other genetic disorders involved with the TCA cycle (e.g. alpha-ketoglutarate dehydrogenase deficiency) with an estimated WW population of ~2,000-5,000 are also promising indications for THN therapy. For patients suffering from these disorders, THN could supply the TCA cycle intermediaries, such as succinyl-CoA/citrate, that they would not be able to synthesize otherwise.

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Sialic Acid-Extended Release – substrate replacement for HIBM

SA-ER (UX001) is an extended release oral formulation (tablets) of a stabilized version of a naturally occurring sugar derivative, Neu5Ac or simply 'sialic acid (SA)'. In fact, Neu5Ac is the most common entity of a class of molecules used within our bodies collectively referred to as sialic acids. RARE is evaluating SA-ER for the treatment of HIBM that is an autosomal recessive neuromuscular disease that presents in early adulthood as weakness in the distal muscles of the lower extremities due to a deficiency in SA and progresses proximally, leading to a loss of muscle strength and function, and ultimately a wheelchair-bound state. Worldwide rights to SA-ER were licensed from Nobelpharma to whom RARE will owe a high single digit royalty on net sales in all regions excluding Japan and certain Asian territories, while Noblepharma will pay RARE a mid-single digit royalty on their sales excluding Japan. RARE estimates that there are ~1,200 - 2,000 patients in the developed world with HIBM of which ~300-400 are in the US and has already identified > 300 patients in the US and >800 patients worldwide. SA-ER is currently in the extension phase of a phase 2 trial in HIBM patients. Data from the 48 week portion of the study was mixed, but we believe the higher total SA dose being studied in the extension phase could result in more consistent and statistically significant clinical improvements. We estimate SA-ER will be launched for HIBM in 2018 generating peak adjusted worldwide sales of $65M.

SAs – Biosynthesis and Role

In general, SA's biological destiny is to modify the structure and biological function of either proteins or lipids, the conjugates of which are referred to as sialoglycoconjugates (SGCs). These SGCs are found throughout the body, especially in the brain and muscle tissue, and it appears that their metabolism, function and distribution are very tissue specific. SA biosynthesis is a relatively complex process which is mediated by at least 9 distinct enzymes. This process can occur in most human tissues and the rate-limiting steps are both performed by GNE/MNK (or uridine diphosphate-N-acetylglucosamine [UDP-GlcNAc] 2-epimerase/N-acetylmannosamine [ManNAc] kinase). The majority of SA production comes from glucose, but a small proportion is derived from ManNAc which trace amounts are passively transported into the cells from the blood-stream. SA may also be imported into cells via endocytosis and then subsequently actively transported into the cytosol from lysosomes. SA-ER is an encapsulated form of SA, which allows for a constant rate of gut-absorption of the SA, and thus a relatively consistent supply of SA for incorporation into SGCs.

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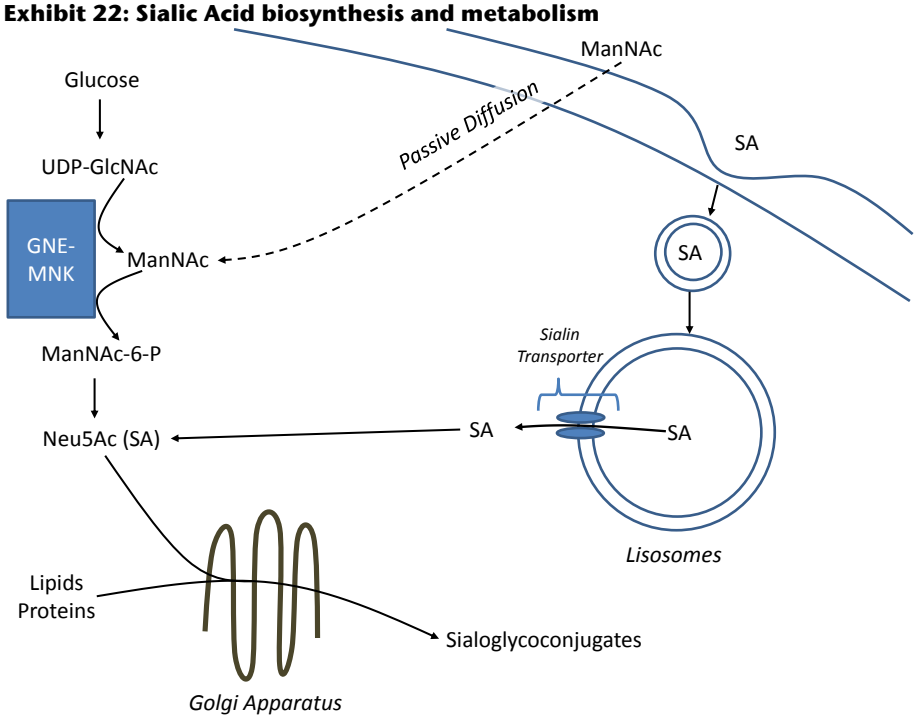
Exhibit 22: Sialic Acid biosynthesis and metabolism



Source: Jefferies

Hereditary Inclusion Body Myopathy (HIBM)

Clinical presentation

HIBM was first characterized in Jews of Persian descent in the 1980s, with a presentation of proximal to distal muscle weakness of both the upper and lower limbs, usually beginning around the age of 20. Since then, HIBM has been found to affect individuals worldwide, with varying racial and ethnic backgrounds. After initial onset, steady progression of muscle weakness and atrophy continues over the next 10-20 years. Typically, the first signs of weakness/atrophy are seen in the legs (particularly in muscles involved with extending the feet), resulting in an abnormal gait. From there, the myopathy spreads to the rest of the leg and also manifests in the shoulders and some of the arm muscles. Amongst myopathies, HIBM appears to have a unique presentation in that it almost completely spares the quadriceps muscles and leaves the biceps and triceps less affected. After 10-15 years of disease progression, patients suffering from HIBM are typically confined to a wheelchair, and in extreme cases may develop cardiomyopathies.

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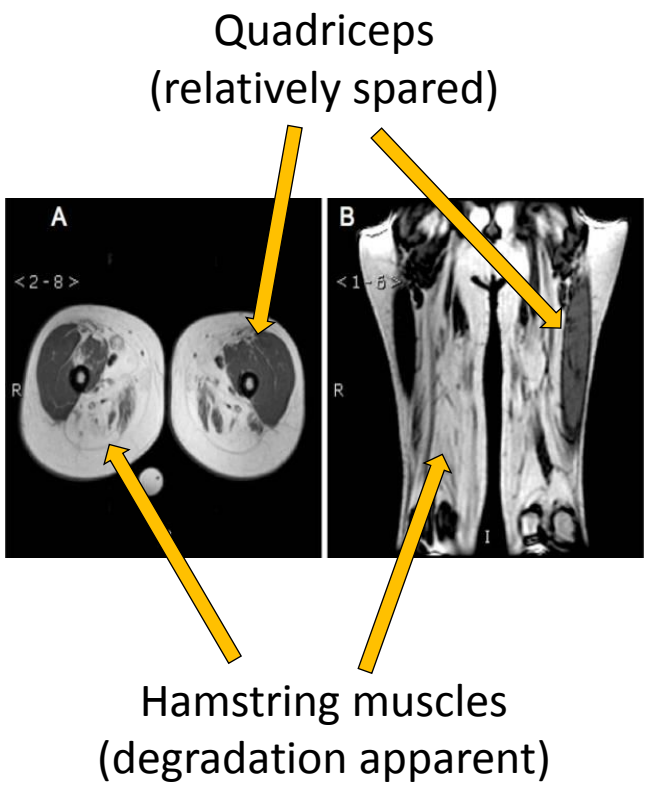
Exhibit 23: HIBM clinical presentation with relative quadriceps sparing



Source: Adapted from Company Data

Genetic basis for HIBM

Genetically, HIBM has been associated with over 62 unique mutations within the *Gne* gene, which encodes for the integral enzyme GNE/MNK within the SA biosynthetic pathway. As the name implies, GNE/MNK has two distinct domains that each catalyze a different process: **1)** conversion of UDP-GlcNAc to ManNAc (GNE domain), and **2)** phosphorylation of ManNAc (MNK domain). Most of the mutations responsible for HIBM occur in the GNE domain (37/62), but research suggests that a mutation in either domain changes overall protein conformation and thus impacts both enzymatic activities.

Given the prominent role of GNE/MNK in SA biosynthesis, most specialists believe the pathophysiology of HIBM is primarily caused by reduced production of SGCs (hyposialation). Support for this hypothesis is provided by *Gne* mutant mouse models, and some anecdotal clinical evidence. *Gne* mouse models, which have similar myopathies to HIBM patients (although striking differences as well, namely nephropathies), have improved muscle strength and myopathic progression is halted when they are supplemented with either SA or ManNAc. In human patients with HIBM, provision of IgG (which has a high SA content) qualitatively improves patients' perception of their condition, but no statistically significant changes in quantitative measures were noted.

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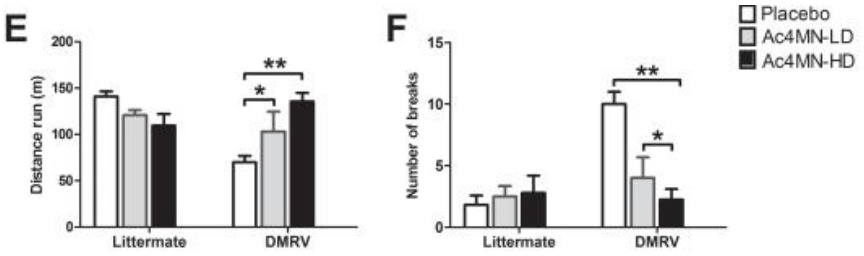
Exhibit 24: ManNAc supplementation improves muscle strength and endurance in a *Gne* mutant mouse



DMRV = Gne mutant mouse
Ac4MN = Oral Acetylated ManNAc
Source: Company Data

Diagnosis and Prevalence

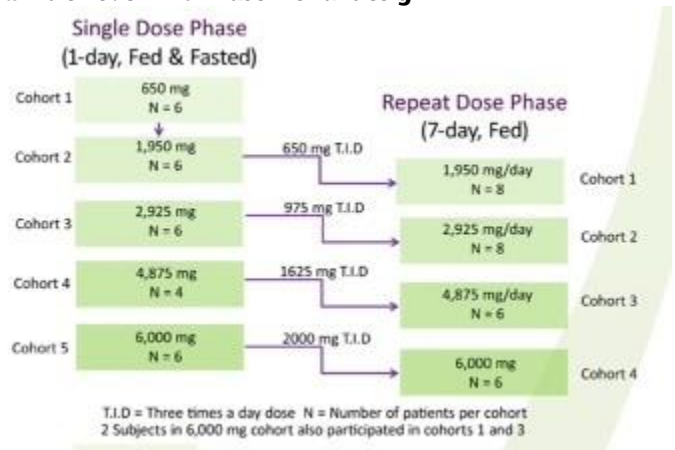
HIBM is diagnosed from a pathologist's evaluation of muscle biopsies, which typically contains autophagic (e.g. digestive) vacuoles, atrophic and/or degenerating muscle fibers. RARE estimates that there are ~1,200 to 2,000 HIBM patients in the developed world of which 300-400 reside in the US. To date, RARE has identified >800 patients worldwide including >300 in the US.

Clinical development of SA-ER for the treatment of HIBM

Phase 1 trial

A phase 1 trial evaluated the safety and pharmacokinetics of orally administered SA-ER in a total of 26 HIBM patients. SA-ER was given as both a single dose (0.65, 1.95, 2.925, 4.875 and 6.0 g) and 7-day repeated dosing (1.95, 2.925, 4.875, and 6.0 g/day divided evenly into 3 doses per day).

Exhibit 25: SA-ER Phase 1 trial design



Source: Company Data

The pharmacokinetic goal of this study was to determine if it would be feasible to provide adequate SA for SGC production over the entire course of a 24 hour period. In all

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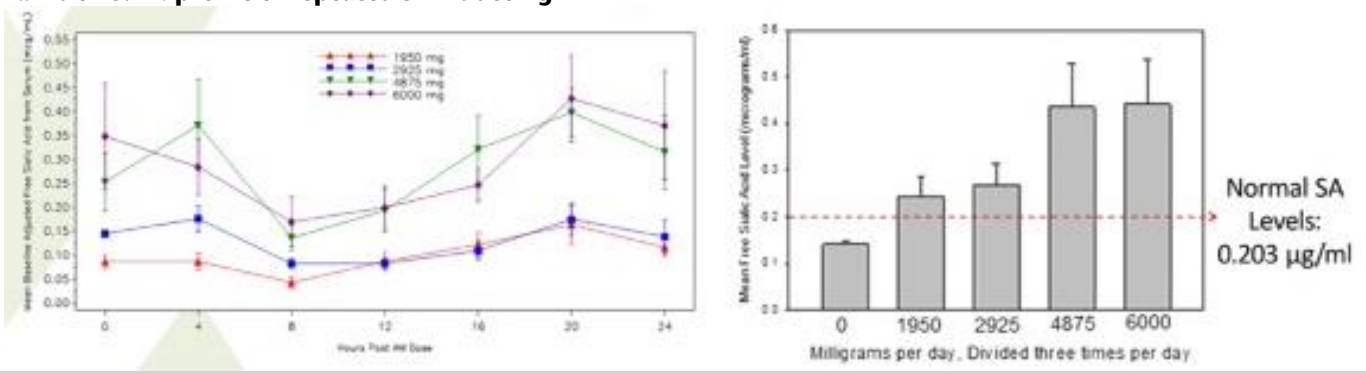
repeated dose treatments, greater than normal levels of SA were achieved, and in the two highest doses (4.875 and 6.0 g/day), this was sustained throughout a 24 hour period. In total, ~62% (16) of the patients experienced at least one AE, but none of these were considered to be treatment related.

Exhibit 26: PK profile of repeated SA-ER dosing

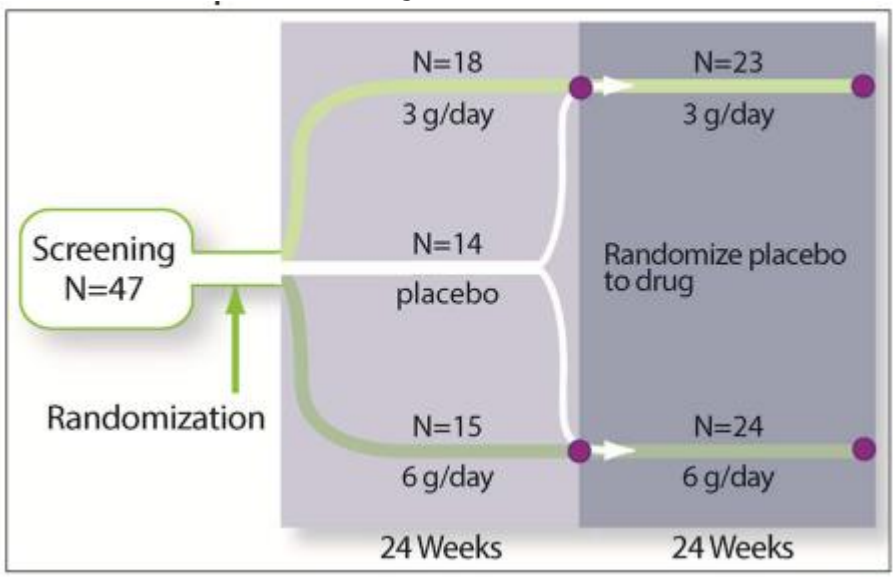


Source: Company Data

Phase 2 trial – SA-ER stabilizes upper extremity muscle strength

At the American Academy of Neurology meeting this year, RARE presented detailed results from its phase 2 trial investigating the safety and efficacy of SA-ER (3 or 6g/day) for the treatment of HIBM in a total of 47 patients. The study was broken into two 24 week periods: 1) a double-blind placebo controlled portion (comparing 3 or 6 g/day vs. placebo); and 2) a cross-over portion where placebo patients were re-randomized into the 3 or 6g/day groups.

Exhibit 27: SA-ER Phase 2 trial design



Source: Company Data

The efficacy endpoints for this study included a composite strength score for both the upper (deltoids, triceps, biceps and grip) and lower (hip extensor/flexors, abductors/adductors and knee flexors [a.k.a. hamstrings]) limbs, walk related measures (e.g. a 6 minute walk test) and a self-reported functional activity score. Safety endpoints included AEs and standard laboratory measures.

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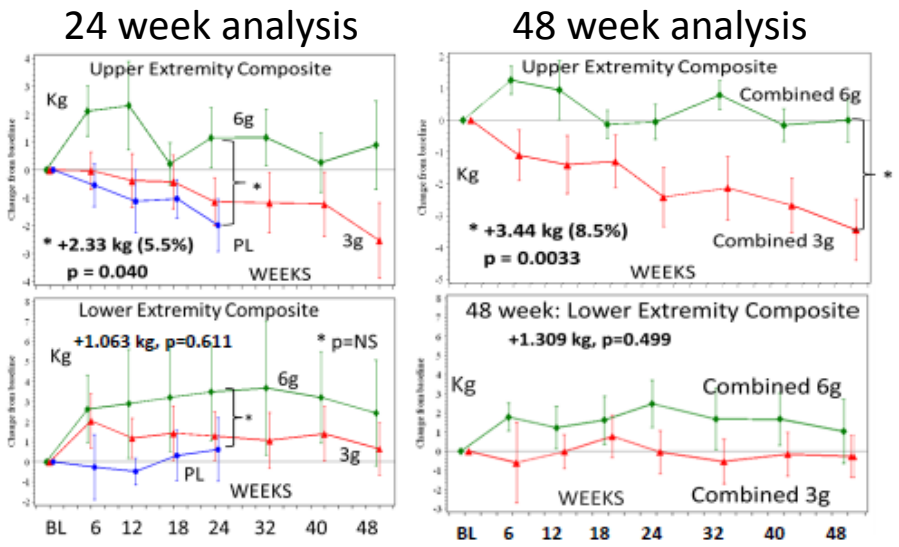
At 24 weeks, there was a dose dependent improvement in muscle strength especially on the upper extremity composite in the 6g group. There was a significant 5.5% improvement (+2.33kg; p=0.04) in upper extremity composite strength vs. placebo in the 6g group, but not the 3g group, when compared to the placebo group. There was a dose dependent improvement in the lower extremity composite with some positive trends in the 6g group vs. placebo (+1.063kg). The treatment effect was more pronounced in a predefined group of patients that had a greater walking ability at baseline (>200m in the 6 min walk test). Creatine kinase levels showed a trend toward improvement in the 6g group vs. placebo but there were no changes observed in any of the other endpoints at 24 weeks. Muscle biopsies that were designed to evaluate SA-ERs effect on protein sialation were inconclusive. At 48 weeks, there was a significant 8.5% improvement in the upper extremity composite score in the combined 6g group vs. the combined 3g group (+3.44kg; p=0.0033). There was no meaningful difference in the lower extremity composite score at 48 weeks (+1.309kg). When qualitatively assessing the trends for the strength scores, it appears that the upper limb strength scores are steadily declining in both the 3g and the placebo groups, but are held constant in the 6g group. In contrast, the lower limb strength scores are relatively constant throughout the study period irrespective of assignment to a placebo or treatment group. This suggests that there is a 'floor-effect' (or the lower limb strength is already at its lowest point) and that treatment should be more effective in patients that do not have full progression of the myopathy. This is supported by muscle strength scores at baseline that were significantly decreased for the upper vs. lower extremity muscles (mean 25% of normal) and corroborated by some improvement or no decline in the placebo or 3g groups. This is also supported by a pre-defined analysis of the upper limb strength scores stratified by severity. When all patients are included, SA-ER treatment improved upper extremity composite strength by 8.5% over baseline, but in less severe patients (e.g. patients that could walk > 200m in the 6 min walk test) this strength was increased by 9.6% over baseline (+4.69kg; p=0.00055).

Exhibit 28: Composite limb strength scores with SA-ER treatment



Source: Company Data

There were positive trends on the GNE myopathy specific patient reported outcome (GNEM-Functional Activity Scale) at 48 weeks in the combined 6g group vs. the combined

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3g group as demonstrated in the total, mobility, and upper extremity endpoints but not the self-care endpoint. There were no statistically significant changes up or down in the walking tests (6MWT, stair climb, walk speed test) or the weighted arm lift test for the combined 6g vs. 3g groups. There was a positive trend for the combined 6g vs. 3g group in the Sit-to-Stand test. There were no dose-dependent treatment emergent AEs or SAEs reported in this study and the most common AEs included procedural pain related to the muscle biopsy and mild to moderate GI related AEs.

Following the dose response seen in this study at 24 and 48 weeks, RARE is continuing an extension study evaluating a new higher dose of 12g/day comprising 6g of SA-ER and 6g of immediate release sialic acid per day for up to an additional 36 months. The extension study is also enrolling an additional 10 treatment naïve patients for a total enrollment of 56 patients. Management says that preliminary data from this study will be presented at the World Muscle Society meeting on October 11.

RARE is consulting with regulatory bodies to determine the next step for the SA-ER clinical program. As part of this process, RARE is evaluating the optimal endpoints, dosage and inclusion criteria for the next study. We believe RARE will have a better idea of the dose (6g or 12g) and endpoints after it has the data from the extension study and the 10 treatment naïve patients. As was seen in the phase 2 study, RARE could decide to include only patients with less advanced disease to allow it to show a more pronounced improvement for SA-ER treatment.

Current treatments for HIBM

No therapies are currently available for HIBM. In the past, some dietary modifications have been proposed: avoidance of excess selenium, copper and zinc (which are all inhibitors of GNE/MNK activity), reduced alcohol consumption (ethanol promotes breakdown of sialoglycoconjugates) and increased consumption of magnesium (an essential co-factor for GNE/MNK). Despite the theoretical basis for these dietary changes, all have yielded little to no efficacy in treating HIBM.

As stated above, many have proposed that supplementation of the by-product of GNE/MNK activity, ManNAc, or the end result of the synthetic pathway, SA, will be effective therapies for HIBM. Both of these strategies have advantages: ManNAc is passively transported into cells, so it does not require endocytosis/liposome active transport (which is inhibited during an autophagic state); SA does not require GNE/MNK processing (or any other processing for that matter) to become integrated into SGCs. Importantly, the pK characteristics of both molecules require a modification or encapsulation (as is the case with SA-ER) to create a constant and sufficient supply of SGCs. Foreseeing this biochemical necessity, RARE owns IP for extended release versions of both molecules. NewZealand Pharma is developing DEX-M74 or ManNAc for HIBM with which a phase 1 study was conducted by the NIH but we do not believe the results have ever been communicated. In either case, these supplements are unlikely to reverse damage done by hyposialation, but will rather be a prophylactic against disease progression. Given these characteristics, proper diagnosis of HIBM as early as possible, paired with a prophylactic therapy will provide the patients with the best possible prognosis.

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Exhibit 29: Comparison of ManNAc and SA supplementation for HIBM

	ManNAc	SA	Comments
Transport into the cell	Passive transport	Endocytosis/active transport	Endocytosis/liposome likely inhibited in autophagic cells
Intracellular processing	Phosphorylation by GNE/MNK required	No processing required	All *Gne* mutations likely affect MNK phosporylation activity
Chemical modifications	Hydrophobic modifications may improve cellular absorption	Proprietary 'ER' modification for improved retention	Unknown how chemical modifications will affect incorporation into sialoglycoconjugates
Clinical Status	Phase 1 complete	Phase 2 ongoing	No current commercial interest in ManNAc, but RARE owns IP for extended release version of both molecules

Source: Jefferies

As stated above, there has been some work (mostly preclinical) evaluating ManNAc as a potential treatment for HIBM. One NIH sponsored Phase 1 PK study has been completed to date, but the data has not been released yet. We view ManNAc as an inferior treatment option to SA because it still requires GNE/MNK activity. While it is true that most mutations to the *Gne* gene are not located within the MNK domain of the protein (the domain that processes ManNAc), research suggests that all mutations inhibit both activities of the protein to varying degrees. Therefore, ManNAc treatment will only have limited efficacy in patients with mutations within the GNE domain (37 of 62 total mutations), and no efficacy in the rest of the patients. However, if SA-ER proves to be inferior for all or a subset of HIBM patients, RARE can pursue an extended release version of ManNAc as an alternative therapeutic.

HIBM Market Opportunity

We assume that SA-ER is launched globally in 2018 at an annualized price of $80,000/patient. We assume that the prevalent population in the US and EU totals ~1,500 HIBM patients and ROW we assume a prevalence rate of 0.11/100K. We estimate peak penetration of 65%, 60% and 10% in the US, EU and ROW, respectively, resulting in peak unadjusted sales of ~$50M, ~$46M and ~$6M in the respective regions. After assuming a 70% probability of success and an 8% royalty rate to NobelPharma, SA-ER can achieve peak WW adjusted sales of ~$65M.

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rhGUS (UX003) for the treatment of MPS VII

rhGUS is a recombinant form of the human protein β-glucuronidase, which is involved in the breakdown of large sugar molecules called glycosaminoglycans (GAGs). rhGUS was developed by researchers at St. Louis University, which is where the deficiency of this enzyme resulting in the autosomal recessive lysosomal storage disorder mucopolysaccharidosis type VII (MPSVII) or 'Sly Syndrome,' was first described. rhGUS is purified from Chinese hamster ovary (CHO) cells, and has been shown to have both 'tagging' signals (mannose and mannose-6-P, see below for details) necessary for uptake into tissues throughout the body. RARE will owe a low single digit royalty on commercial sales to St. Louis University after reaching $10M of cumulative worldwide sales. While there are no issued patents covering rhGUS, the drug has received orphan drug designation in the US and EU. Proof of concept in humans has so far come from a single patient that was treated under an emergency IND and interim data from an ongoing phase 1/2 trial. RARE plans to initiate a phase 3 study by YE14 based on positive interim data from the phase 1/2 study and 24 week data from the single patient under the eIND. An open label study in patients < 5 years old including those with Hydrops fetalis (MPS VII at birth) is planned. We forecast rhGUS adjusted WW peak sales in MPS VII of $57M.

MPS VII Background

Lysosomes – the cellular 'cleaning crew'

Through the course of normal metabolic processes, all cells in our bodies produce a variety of waste products that need to be broken down. Disposal of these waste products is performed by lysosomes, or spherical structures that contain a variety of catabolic enzymes in an acidic environment (pH ~5). These catabolic enzymes, often referred to as lysosomal enzymes, may be produced within the cell's own endoplasmic reticulum, or alternatively they may also be imported from the circulation via endocytosis. When these enzymes are produced, a sugar residue (mannose or Man) is added, and this may be further modified or 'tagged' with a phosphate group (mannose-6-phosphate or M6P). These modifications to both intracellular and extracellular lysosomal enzymes facilitate their integration into the lysosomes, and in the case of the extracellular variety allow them to be taken up by the cell. Endocytosis of lysosomal enzymes is mediated by receptors that recognize either Man (Mannose receptors, MR) or M6P (M6P receptors, M6PR). Distribution of these receptors appears to be tissue specific. For example, brain and muscle preferentially express M6PR, whereas the spleen and the liver express more of MR. Therefore, in order for an extracellular lysosomal enzyme to be taken up by all tissues in the body, it must be ' tagged' with both Man and M6P.

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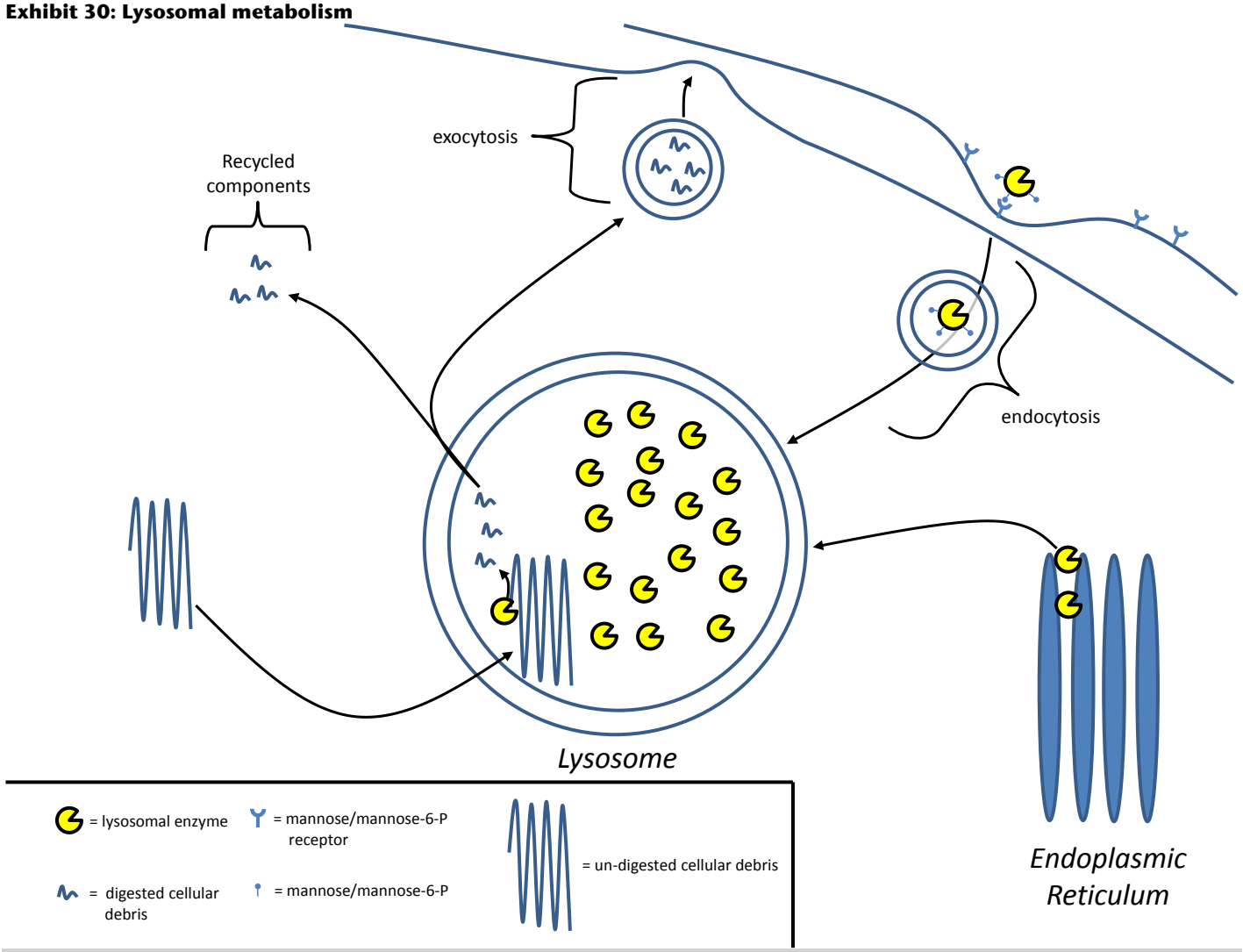
Exhibit 30: Lysosomal metabolism



Source: Jefferies

MPS VII – A forgotten Lysosomal Storage Disorder

MPS VII or Sly Syndrome is caused by a mutation to the *Gusb* gene, which encodes for the protein β-glucuronidase. These mutations can range in severity from just reducing to completely eliminating the enzymatic activity. In either case, the autosomal recessive inheritance of this deficiency in β-glucuronidase leads to an excess accumulation of its substrate (the GAGs dermatan sulfate and heparin sulfate that are critical components of many tissues) within the lysosomes throughout the body. This GAG accumulation eventually leads to expansion of the lysosomes, which in turn causes the organs themselves to expand. Research also suggests that high concentrations of GAGs also inhibit other lysosomal enzymatic activity, thus leading to a buildup of other cellular waste in addition to GAGs which are typically excreted in urine.

Clinically, MPS VII typically presents with enlarged liver and spleen, airway and pulmonary disease, heart valve disease, bone and joint abnormalities (short stature and abnormal skeletal features), unusually 'coarse' facial features and mental retardation. Onset of symptoms is typically early in life, and usually results in death by the teenage years, but survivorship has been noted as late as the age of 30. In the most extreme cases,

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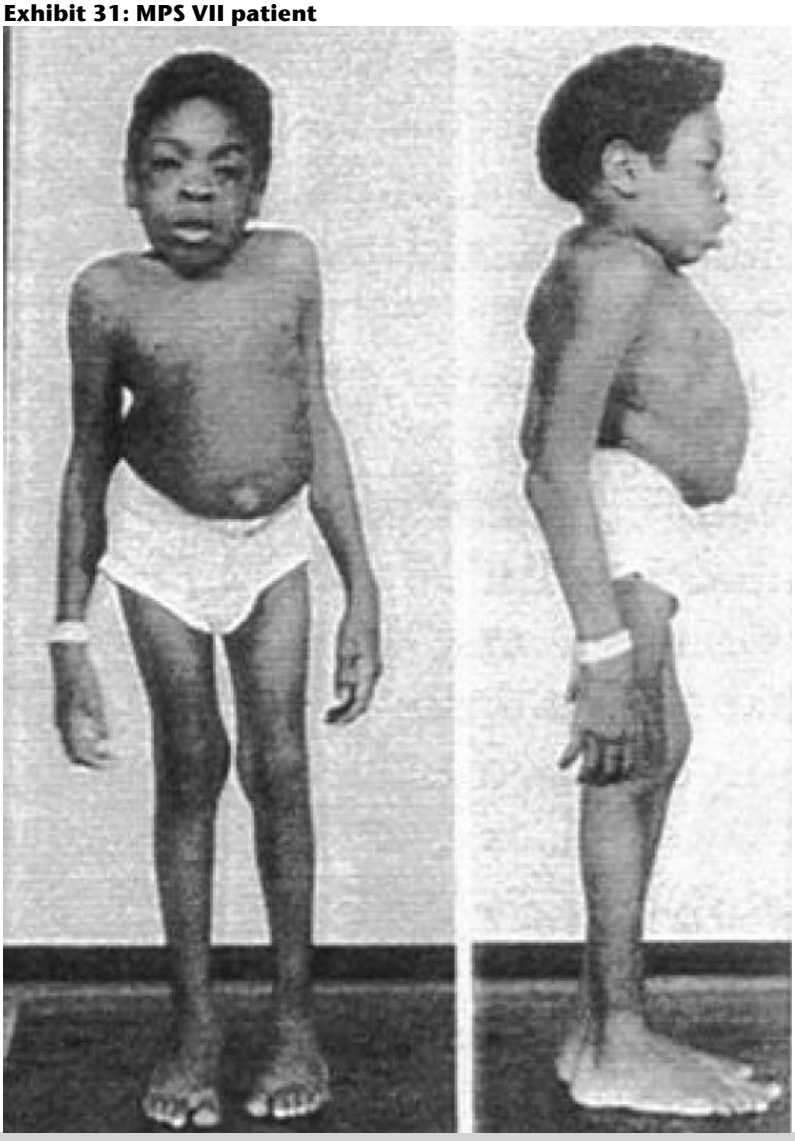
MPS VII presents at birth with the child retaining an enormous quantity of fluid in a state commonly referred to as non-immune hydrops fetalis or simply 'hydrops.' Infants with hydrops fetalis rarely survive longer than a few weeks or months.

Diagnosis and Prevalence of MPS VII

Diagnosis of MPS VII starts with the typical presentation of symptoms consistent with a MPS disorder (e.g. stiffened joints, respiratory problems, heart defects and enlarged organs), followed by a urinary measure of GAGs over that of normal levels. If urinary GAGs are increased, enzymatic assays of cultured cells (leukocyte enzyme assays) from the patient are used to confirm the specific pathway that is involved with the particular MPS the patient is suffering from. Prenatal diagnosis is also possible by assessing GAG concentrations and enzymatic activity from an amniocentesis.

MPSVII is one of the rarest forms of lysosomal storage disease, with a predicted number of ~200 patients in the developed world, and a predicted incidence rate of 1 out of every 250,000 births. ~20 patients per year are born with hydrops fetalis and RARE has thus far identified 91 MPS VII patients worldwide (15 of these in the US).

Exhibit 31: MPS VII patient



Source: Company reports

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Preclinical/Clinical experience with rhGUS

Preclinical data

RARE has demonstrated rhGUS production at a large scale in CHO cells and the enzyme has demonstrated a long intracellular half-life (~40 days) and high affinity uptake (Kuptake ~1.9nM) in MPS VII fibroblasts. Toxicology studies showed that rhGUS was well tolerated in juvenile monkeys and MPS VII mice when administered at 2, 6, and 20 mg/kg via a 2hr IV infusion. After 8 weeks of treatment with rhGUS in MPS VII mice, urinary GAG (uGAG) levels and lysosomal storage were decreased in a dose dependent manner (> 80% reduction at some doses). Importantly, RARE was able to achieve uptake within the target tissues including brain, bone, heart, kidney, liver, lung, muscle, and spleen.

Treatment of a single patient using an eIND

Data of rhGUS treatment in a single patient using an emergency IND (eIND) was presented at the Annual World Lysosomal Disease Network Symposium in Feb 2014. The patient was a 12 year old boy with a confirmed diagnosis of MPS VII by the age of 17 months. Symptomatically, he had an enlarged spleen and liver, significant heart valve abnormalities, spinal cord compression (which necessitates wheelchair use), frequent fatigue and increasing pulmonary difficulties. Immediately preceding rhGUS treatment, he required two hospitalizations and constant ventilator use, events which led to the eIND.

rhGUS (2mg/kg) was given to the patient as an IV infusion over 4-5 hours every 2 weeks, and the patient was followed for 14 weeks or 8 infusions. Immediately following rhGUS treatment, uGAG excretion (50% reduction), and liver and spleen volumes were reduced suggestive of lysosomal storage clearance. The patient was less fatigued and decreased sleeping during the day, his stamina improved, and he began to manipulate the wheelchair independently again. There was an improvement in pulmonary function as evidenced by reduced dependence of the patient on ventilator support (able to tolerate monitored breaks from the constant ventilator use) and lowered carbon dioxide retention. The patient did not suffer from any treatment emergent serious adverse events, although 'hive-like' symptoms were noted within 24 hours following the first and second infusion that was improved with Atarax use. There were no infusion associated reactions during the 14 weeks but the patient did have temporary fatigue 24-48 hours post infusions. This was thought to be due to secondary fluid overload related to the patient's valve disease but it improved with treatment.

In a recent update during the SSIEM conference in September, RARE noted that after 24 weeks of treatment a 50-70% reduction in uGAG excretion was observed in this patient and reduction in the size of the enlarged liver and spleen were maintained. Improved pulmonary function based on reduced carbon dioxide retention continued to be observed.

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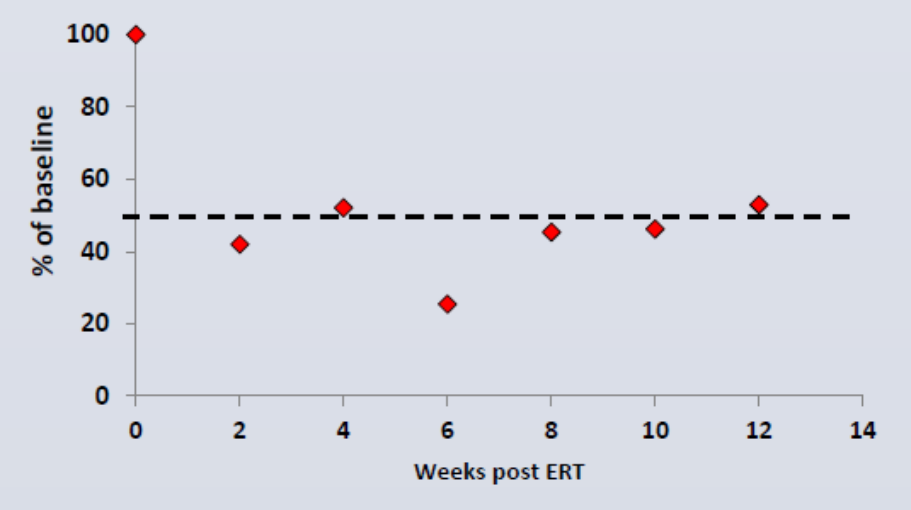
Exhibit 32: Total uGAG levels reduced following rhGUS infusions

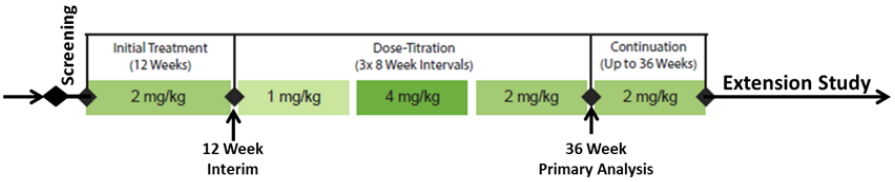


Source: Company Data

Ongoing Phase1/2 trial

Following positive results from the single patient, in December 2013 RARE initiated a full phase 1/2 open label study to evaluate the safety, efficacy, and dose of rhGUS in 5 patients aged 5-30 years including 2 aged 20-30 years. Patients also had to have a confirmed diagnosis via a leukocyte enzyme assay or a genetic test, uGAG excretion > 2x normal, and no history of a successful bone marrow transplant. This study is also expected to evaluate the biochemical and clinical proof of concept of rhGUS in MPS VII. The open-label study has 3 distinct treatment intervals (all with IV infusions once every other week): Initial treatment – 2mg/kg for 12 weeks after which there will be an interim look; dose titration – 1mg/kg, 2mg/kg and 4mg/kg (each for 8 weeks for total 24 weeks); and treatment continuation – 2mg/kg or 'optimal dose' for another 28 weeks. The primary endpoint for the study is total uGAG excretion at 36 weeks and the secondary endpoints include six minute walk test, three minute stair climb, pulmonary function assessed by spirometry, growth velocity (height and weight), and shoulder range of motion. Safety will be assessed using a composite of AEs and clinical laboratory measures.

Exhibit 33: Ongoing Phase 1/2 rhGUS trial design



Source: Company Data

To date, 3 patients have been enrolled in the study, and preliminary data were presented at the ACMG meeting in Mar 2014. Total uGAG was reduced from baseline by 30-50% in all 3 patients post infusions. One of these patients (#201) received all 7 rhGUS infusions over 12 weeks after which reductions in hepatomegaly using various measures was demonstrated. There were no SAEs and no infusion associated reactions reported after 13 total infusions.

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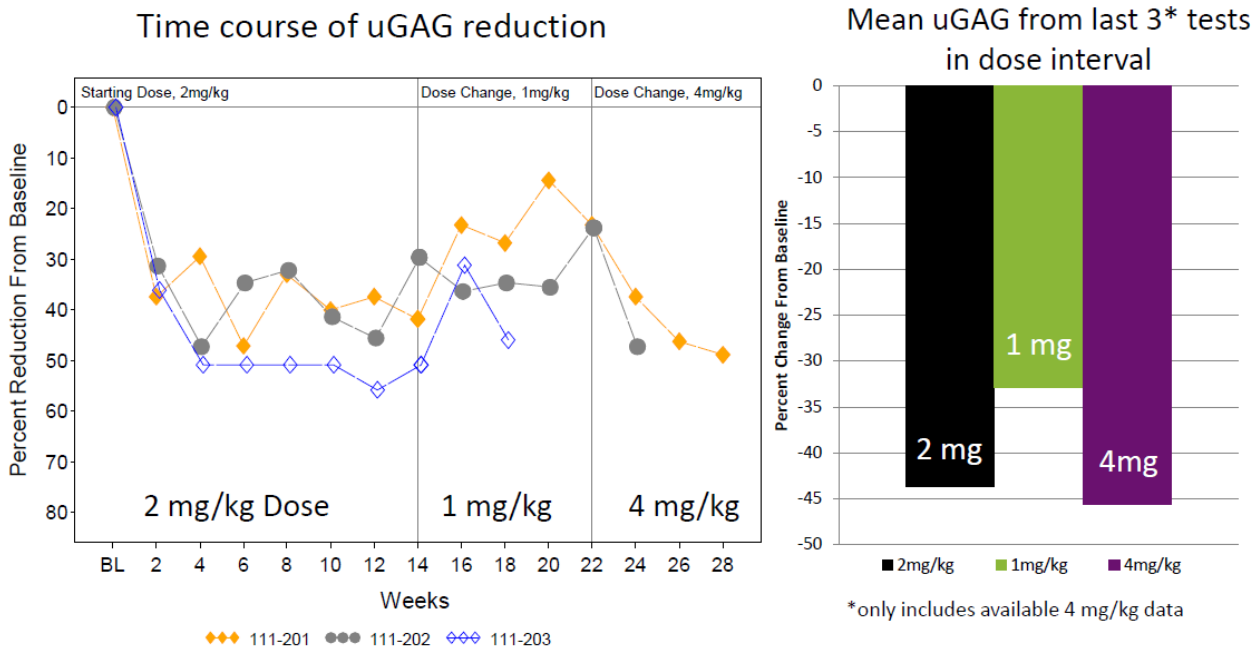
Updated data on these patients was presented at the SSIEM meeting in Sept. 2014. Reductions in uGAG excretion levels occurred rapidly after the first dose (2 weeks after the first dose), was sustained (40-50% from baseline after 12 weeks), and was dose dependent (an increase in uGAG on the lower 1mg/kg dose). Two patients with hepatomegaly at baseline had their liver volumes decrease significantly at 12 weeks as determined by ultrasound. The third patient did not have a baseline scan and was subjectively reported as having no change from baseline in hepatomegaly at 12 weeks. Clinical measures like the 6 minute walk test were inconclusive and might require assessment after longer term treatment to observe any clinical benefit. There were no SAEs reported up to 28 weeks of treatment with no drug related or infusion associated reactions. AEs reported were infections and GI disorders that were not considered related and there was no significant increase in immune response to the rhGUS enzyme with additional data pending.

Future development plans

RARE has already agreed with the EMA on a phase 3 trial in 12 patients with a blind start design that will evaluate uGAG as the primary endpoint, which the EMA has agreed to assuming some benefit on the clinical endpoints. We believe further discussions with the FDA regarding the use of uGAG as an appropriate primary endpoint and the size of the trial will determine the path forward in the US. We believe data from the ongoing phase 1/2 study (12 week interim) could help demonstrate the linkage of uGAG levels with other clinical endpoints. RARE also plans to initiate a study of rhGUS in MPS VII patients < 5 years old including those with hydrops fetalis.

Exhibit 34: Effects of rhGUS on uGAG levels



Source: Company Data

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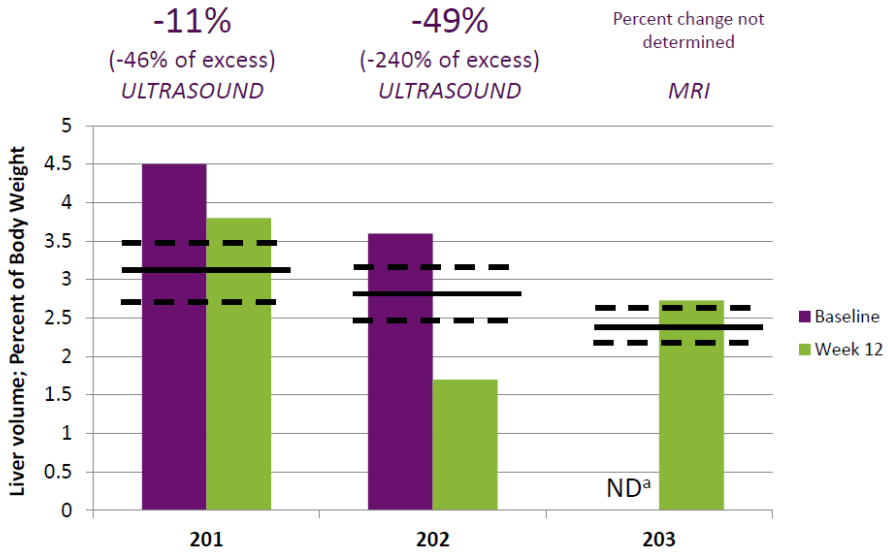
Exhibit 35: Effects of rhGUS on Liver Volume



Source: Company Data

Current treatments for MPS VII

There are no treatments currently available for MPS VII. Dietary changes, such as reducing dairy intake or foods with 'excessive' additives, have anecdotally relieved gastrointestinal symptoms in some patients, despite these measures having no scientific basis. Physical therapy, especially passive stretching and other range of motion exercises, improve symptoms of joint stiffness and pain in most patients. Both bone marrow transplant (paired with a gene therapy) and enzyme replacement therapy have been employed experimentally in mouse models of MPS VII, but rhGUS is the first therapy to enter the clinic. We are unaware of any other potential treatments for MPS VII. Theoretically, a gene therapy approach would be possible, but we are not aware of any efforts that may be underway either commercially or academically.

MPS VII Market Opportunity

We assume that rhGUS is launched globally in 2017 at an annualized price of $450,000/patient that remains flat and patent expiration in 2027. We assume that the prevalent population in the US and EU totals ~200 MPS VII patients and ROW we assume a prevalence rate of 0.011/100K. We estimate peak penetration of 80%, 70% and 15% in the US, EU and ROW, respectively, resulting in peak unadjusted sales of ~$37M, ~$40M and ~$6M in the respective regions. After assuming a 70% probability of success and a 2% royalty rate to St. Louis University, rhGUS can achieve peak WW adjusted sales of ~$57M.

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rhPPCA (UX004) – preclinical LSD candidate for the treatment of galactosialidosis

rhPPCA was licensed from St. Jude's in Sept 2012 for the treatment of Galactosialidosis (GSLD) and other monogenic diseases for which RARE will owe a <1% royalty to St. Jude's on net sales. GSLD, like MPS VII, is a rare autosomal recessive lysosomal storage disorder. In GSLD however, these mutations are not within the genes that encode for the actual lysosomal enzymes, but rather in the CTSA gene that encodes a protein called protective protein/cathepsin A (PPCA) that protects and stabilizes these enzymes (sialidase and beta-galactosidase). The deficiency in PPCA thus causes a subsequent decrease in activity of these other lysosomal enzymes, and symptomatically is similar to other lysosomal storage disorders with a buildup of substrate oligosaccharides in the lysosomes. This buildup of oligosaccharides impacts organs like the liver, spleen, and other tissues as well as bone and cartilage. Mice and in vitro studies have demonstrated a reduction in the storage of oligosaccharides in multiple organs with PPCA administration.

GSLD varies in time of onset, and is categorically labeled as early infantile (between birth and 3 months of age), late infantile (begins in the first few months of life and life expectancy can vary depending on severity of symptoms) or juvenile/adult (onset at 16 years of age), with the severity of the PPCA mutation inversely correlated with the age of onset. 70-80% of GSLD patients have the late infantile and juvenile/adult type. The prevalence of GSLD is unknown, but only ~100 cases have been described clinically to date in the developed world although actual estimates could be much higher. RARE estimates that there are ~300-500 GSLD patients in the developed world.

There is currently no available treatment for rhPPCA apart from bone marrow/stem cell transplants used for other LSDs. Despite the slightly different pathophysiology, the strategy for rhPPCA treatment is essentially the same as that for rhGUS. rhPPCA will be infused in patients with GSLD, and if it is appropriately incorporated into the lysosomes of these patients it should increase enzymatic activity of sialidase and beta-galactosidase. rhPPCA is currently undergoing preclinical evaluation for toxicity and pharmacokinetics. We do not expect rhPPCA to enter the clinic until 2015/2016.

We do not assign any value to rhPPCA in our model at this time given it is still in preclinical development.

Financials

As of 2Q14, RARE had $162.6M cash and cash equivalents on hand, which management expects to last to YE16. We have assumed a $200M financing at $74 on 2.7M shares in 2016.

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Managment

Emil D. Kakkis, M.D., Ph.D., **President and Chief Executive Office**r. Dr. Kakkis has been a member of the Board since inception in April 2010. Prior to Ultragenyx, Dr. Kakkis served from September 1998 to February 2009 in various executive capacities, and ultimately as Chief Medical Officer, at BioMarin Pharmaceutical Inc., a biopharmaceutical company. Dr. Kakkis also serves as President and Founder of EveryLife Foundation for Rare Diseases, a non-profit organization he started in 2009 to accelerate biotechnology innovation for rare diseases. Dr. Kakkis is board certified in both Pediatrics and Medical Genetics. He holds a B.A. in Biology from Pomona College and received combined M.D. and Ph.D. degrees from the UCLA School of Medicine's Medical Scientist Training Program where he received the Bogen prize for his research.

Thomas Kassberg, **Chief Business Officer and Senior Vice President.** Prior to Ultragenyx, Mr. Kassberg worked as Vice President of Business Development at Corium International, Inc., a biotechnology company, from July 2010 until October 2011. Prior to his work at Corium International, Inc., Mr. Kassberg worked as an independent consultant in Corporate Development and Business Strategy and consulted with a number of companies from March 2009 to June 2010, including Corium International, Inc. and Rib-X Pharmaceuticals, Inc., a pharmaceutical company focused on the development of novel antibiotics. Before becoming a consultant, Mr. Kassberg worked at Proteolix, Inc., a biotechnology company subsequently acquired by Onyx Pharmaceuticals, from January 2008 until February 2009, where he served as Senior Vice President of Corporate Development. Mr. Kassberg holds a B.A. in Business Administration from Gustavus Adolphus College and an M.B.A. from Northwestern University.

Shalini Sharp, **Chief Financial Officer and Senior Vice President**. Prior to Ultragenyx, Ms. Sharp served in various executive capacities, and ultimately as Chief Financial Officer, of Agenus Inc., a biotechnology company, from August 2003 until May 2012. Prior to Agenus, Ms. Sharp held strategic planning and corporate finance roles and ultimately served as chief of staff to the chairman of the board at Elan Pharmaceuticals, a biotechnology company, from August 1998 to August 1999 and September 2001 to August 2003. Prior to Elan, Ms. Sharp was a management consultant at McKinsey & Company and an investment banker at Goldman Sachs, specializing in pharmaceuticals and medical devices. Ms. Sharp has also served as a board member of Agenus since May 2012. Ms. Sharp holds a B.A. and an M.B.A. from Harvard University.

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Exhibit 36: RARE Income Statement: 2013A-2020E ($M)

(In Millions, except per share data)	2013A	1Q14A	2Q14A	3Q14E	4Q14E	2014E	2015E	2016E	2017E	2018E	2019E	2020E
Revenues												
KRN23 (WW)	-	-	-	-	-	-	-	-	-	29.0	64.9	115.7
THN for FAOD	-	-	-	-	-	-	-	-	-	49.1	117.4	190.5
THN for GLUT1	-	-	-	-	-	-	-	-	-	47.5	113.4	202.1
rhGUS	-	-	-	-	-	-	-	-	4.9	10.2	20.1	32.4
SA-ER	-	-	-	-	-	-	-	-	-	6.0	19.4	33.7
Total Revenues	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**4.9**	**141.8**	**335.3**	**574.4**
Operating Expenses												
COGS	-	-	-	-	-	-	-	-	0.7	19.1	45.6	77.3
% of sales	*N/M*	*N/M*	*N/M*	*N/M*	*N/M*	*N/M*	*N/M*	*N/M*	*15%*	*13%*	*14%*	*13%*
R&D	27.8	8.4	11.2	11.2	11.2	42.1	55.0	65.0	75.0	75.0	75.0	75.0
% of sales	*N/M*	*N/M*	*N/M*	*N/M*	*N/M*	*N/M*	*N/M*	*N/M*	*1518%*	*53%*	*22%*	*13%*
SG&A	4.5	2.0	2.4	2.7	2.9	10.0	15.0	20.0	35.0	55.0	75.0	85.0
% of sales	*N/M*	*N/M*	*N/M*	*N/M*	*N/M*	*N/M*	*N/M*	*N/M*	*709%*	*39%*	*22%*	*15%*
Total Operating expenses	**(32.3)**	**(10.3)**	**(13.7)**	**(13.9)**	**(14.1)**	**(52.1)**	**(70.0)**	**(85.0)**	**(110.7)**	**(149.1)**	**(195.6)**	**(237.3)**
Net Operating Income (Expense)	**(32.3)**	**(10.3)**	**(13.7)**	**(13.9)**	**(14.1)**	**(52.1)**	**(70.0)**	**(85.0)**	**(105.8)**	**(7.3)**	**139.7**	**337.1**
Other Income (Expense)												
Interest income	0.2	0.1	0.1	0.1	0.1	0.5	0.5	0.5	0.6	0.6	0.6	0.6
Interest expense	-	-	-	-	-	-	-	-	-	-	-	-
Other expense, net	(3.0)	(3.4)	(0.1)	(0.1)	(0.1)	(3.6)	(3.6)	(3.6)	(3.7)	(3.7)	(3.7)	(3.8)
Total Other Income (Expense)	**(2.8)**	**(3.3)**	**0.1**	**0.1**	**0.1**	**(3.1)**	**(3.1)**	**(3.1)**	**(3.1)**	**(3.2)**	**(3.2)**	**(3.2)**
Income before taxes	(35.1)	(13.6)	(13.6)	(13.9)	(14.1)	(55.1)	(73.1)	(88.1)	(108.9)	(10.5)	136.5	333.9
Taxes	-	-	-	-	-	-	-	-	-	-	(6.8)	(40.1)
Tax Rate	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*0%*	*5%*	*12%*
Net Income (Loss)	**(35.1)**	**(13.6)**	**(13.6)**	**(13.9)**	**(14.1)**	**(55.1)**	**(73.1)**	**(88.1)**	**(108.9)**	**(10.5)**	**129.7**	**293.8**
Basic EPS	(10.37)	(0.63)	(0.45)	(0.44)	(0.44)	(1.74)	(2.30)	(2.56)	(3.15)	(0.30)	3.73	8.43
Diluted EPS	(10.37)	(0.45)	(0.41)	(0.40)	(0.40)	(1.58)	(2.08)	(2.33)	(2.88)	(0.28)	3.40	7.69
Shares outstanding (Basic)	3.4	21.6	30.1	31.7	31.7	31.7	31.8	34.5	34.6	34.7	34.8	34.9
Shares outstanding (Diluted)	3.4	30.1	33.0	35.0	35.0	35.0	35.1	37.8	37.9	38.0	38.1	38.2

Source: Company Data and Jefferies

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Exhibit 37: RARE Balance Sheet: 2013A-2020E ($M)

	2013A	2014E	2015E	2016E	2017E	2018E	2019E	2020E
Assets								
Current assets								
Cash and cash equivalents	7.4	83.5	118.4	240.2	141.1	140.4	279.8	583.3
Short-term investments	46.0	108.3	9.1	9.1	9.0	9.0	8.9	8.9
Cash, cash equivalents and marketable securities	53.4	191.7	127.5	249.2	150.1	149.4	288.7	592.1
Accounts receivable, net	-	-	-	-	-	-	-	-
Prepaid expenses and other current assets	1.8	4.9	5.0	5.0	5.1	5.1	5.2	5.2
Total current assets	55.2	196.7	132.5	254.3	155.2	154.5	293.9	597.4
Long-term assets								
Property and equipment, net	1.3	4.0	6.0	7.0	8.1	9.3	10.6	12.0
Long-term securities	0.5	0.7	0.8	0.8	0.9	0.9	0.9	1.0
Other non-current assets	2.6	1.1	1.2	1.2	1.3	1.4	1.4	1.5
Total assets	**59.6**	**202.5**	**140.4**	**263.3**	**165.4**	**166.0**	**306.8**	**611.9**
Liabilities and Stockholders' Equity								
Current liabilities								
Accounts payable	1.4	3.6	3.6	3.7	3.7	3.7	3.8	3.8
Accrued liabilities	4.4	5.3	5.3	5.4	5.4	5.5	5.5	5.6
Other current liabilities	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1
Total current liabilities	5.9	8.9	9.0	9.1	9.2	9.3	9.4	9.5
Long-term liabilities								
Other long-term liabilities	0.2	0.6	0.6	0.6	0.6	0.6	0.6	0.6
Convertible preferred stock warrant liability	3.4	-	-	-	-	-	-	-
Total long-term liabilities	3.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6
Total liabilities	**9.5**	**9.5**	**9.6**	**9.7**	**9.8**	**9.9**	**10.0**	**10.1**
Commitments and contingencies								
Stockholders' equity								
Preferred stock	124.9	-	-	-	-	-	-	-
Common stock	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Additional paid-in capital	-	259.6	260.1	260.6	261.1	261.6	262.1	262.6
Accumulated other income	0.0	(0.0)	(0.0)	(0.0)	(0.0)	(0.0)	(0.0)	(0.0)
Accumulated deficit	(74.8)	(66.5)	(129.2)	(6.9)	(105.4)	(105.4)	34.8	339.3
Total stockholders' equity	50.1	193.0	130.8	253.6	155.7	156.2	296.9	601.8
Total liabilities and stockholders' equity	**59.6**	**202.5**	**140.4**	**263.3**	**165.4**	**166.0**	**306.8**	**611.9**

Source: Company Data and Jefferies

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Exhibit 38: RARE Cash Flow Statement: 2013A-2020E ($M)

	2013A	2014E	2015E	2016E	2017E	2018E	2019E	2020E
Operating activities								
Net loss	(35.1)	(55.1)	(73.1)	(88.1)	(108.9)	(10.5)	129.7	293.8
Adjustments to reconcile net loss to net cash provided by (used in) operating activities								
Depreciation and amortization	0.4	0.6	0.6	0.6	0.6	0.6	0.6	0.6
Noncash interest expense	-	-	-	-	-	-	-	-
Amortization of premium on investment securities	1.4	3.2	3.2	3.2	3.2	3.2	3.2	3.2
Stock-based compensation	0.7	3.6	3.6	3.6	3.6	3.6	3.6	3.6
Revaluation of convertible preferred stock warrant liability	2.9	3.3	-	-	-	-	-	-
Changes in operating assets and liabilities								
Accounts receivable	-	-	-	-	-	-	-	-
Prepaid expenses and other current assets	(1.6)	(4.5)	(4.6)	(4.6)	(4.6)	(4.7)	(4.7)	(4.8)
Other Assets	(2.6)	0.4	0.4	0.4	0.4	0.4	0.4	0.4
Accounts payable	0.2	1.8	1.8	1.8	1.8	1.8	1.8	1.9
Accrued expenses and other liabilities	2.4	6.1	6.1	6.1	6.2	6.2	6.3	6.4
Net cash provided by (used in) operating activities	**(31.2)**	**(40.7)**	**(62.0)**	**(77.0)**	**(97.7)**	**0.7**	**140.9**	**305.1**
Investing activities								
Purchases of property and equipment	(0.4)	(2.6)	(2.0)	(1.0)	(1.1)	(1.2)	(1.3)	(1.4)
Purchase of investments	(64.0)	(129.3)	(0.1)	(4.5)	(4.6)	(4.7)	(4.8)	(4.9)
Proceeds from maturities of investments	16.6	67.0	99.2	4.5	4.6	4.7	4.8	4.9
Increase in restricted cash	0.0	(0.3)	(0.3)	(0.3)	(0.3)	(0.3)	(0.3)	(0.3)
Net cash provided by (used in) investing activities	**(47.7)**	**(65.2)**	**96.8**	**(1.2)**	**(1.3)**	**(1.4)**	**(1.5)**	**(1.6)**
Financing activities								
Net proceeds from issuance of convertible preferred stock	-	(4.3)	-	-	-	-	-	-
Net proceeds from issuance of common stock	0.2	186.3	-	200.0	-	-	-	-
Proceeds from issuance of promissory notes	-	-	-	-	-	-	-	-
Net cash provided by financing activities	**0.2**	**182.0**	**-**	**200.0**	**-**	**-**	**-**	**-**
Net increase (decrease) in cash and cash equivalents	(78.8)	76.1	34.9	121.8	(99.1)	(0.7)	139.4	303.5
Cash and cash equivalents at beginning of period	86.2	7.4	83.5	118.4	240.2	141.1	140.4	279.8
Cash and cash equivalents at end of period	7.4	83.5	118.4	240.2	141.1	140.4	279.8	583.3

Source: Company Data and Jefferies

Exhibit 39: RARE DCF Analysis

(in millions, except per share data)	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E
EBIT	(70.0)	(85.0)	(105.8)	(7.3)	139.7	337.1	533.2	673.4	725.3	755.8	781.8	641.0	588.2	442.0	300.4	110.5
-Taxes	-	-	-	-	(7.0)	(40.5)	(106.6)	(168.4)	(217.6)	(226.8)	(234.5)	(192.3)	(176.4)	(132.6)	(90.1)	(33.1)
+Depreciation and Amortization	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.7	0.7	0.7	0.7	0.7	0.7	0.7	0.7
-Change in working capital	3.6	3.7	3.7	3.7	3.8	3.8	3.9	3.9	3.9	4.0	4.0	4.0	4.1	4.1	4.2	4.2
-Capital expenditures	(2.0)	(1.0)	(1.1)	(1.2)	(1.3)	(1.4)	(1.5)	(1.6)	(1.7)	(1.8)	(1.9)	(2.0)	(2.1)	(2.2)	(2.3)	(2.4)
Unlevered free cash flow	(67.8)	(81.7)	(102.6)	(4.2)	135.8	299.7	429.5	508.0	510.6	531.9	550.0	451.4	414.4	312.0	212.9	79.8

Source: Jefferies

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Exhibit 40: KRN23 for XLH Market Model

	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E
UNITED STATES (US)													
XLH Cases (total)	15,135	15,286	15,439	15,593	15,749	15,907	16,066	16,226	16,389	16,552	16,718	16,885	17,054
XLH Cases (adult)	11,351	11,464	11,579	11,695	11,812	11,930	12,049	12,170	12,291	12,414	12,538	12,664	12,790
KRN23 market share (adult)	3%	5%	10%	15%	18%	18%	18%	18%	18%	18%	18%	18%	9%
KRN23 patients (adult)	341	573	1,158	1,754	2,126	2,147	2,169	2,191	2,212	2,235	2,257	2,279	1,151
XLH Cases (ped)	3,784	3,821	3,860	3,898	3,937	3,977	4,016	4,057	4,097	4,138	4,179	4,221	4,263
KRN23 market share (ped)	5%	15%	25%	35%	45%	55%	65%	70%	70%	70%	70%	70%	40%
KRN23 patients (ped)	189	573	965	1,364	1,772	2,187	2,611	2,840	2,868	2,897	2,926	2,955	1,705
Price/patient/yr ('000)	85	88	90	93	96	99	101	105	108	111	114	118	121
US KRN23 revenue ($M)	**45.1**	**100.3**	**191.4**	**289.6**	**372.9**	**427.1**	**485.1**	**525.9**	**547.0**	**569.2**	**592.1**	**615.8**	**346.1**
RARE US Royalty (%)	*27%*	*27%*	*27%*	*27%*	*27%*	*27%*	*27%*	*27%*	*27%*	*27%*	*27%*	*27%*	*27%*
RARE US Royalties ($M)	**12.2**	**27.1**	**51.7**	**78.2**	**100.7**	**115.3**	**131.0**	**142.0**	**147.7**	**153.7**	**159.9**	**166.3**	**93.5**
EUROPE (EU)													
XLH Cases	22,702	22,929	23,158	23,390	23,624	23,860	24,098	24,339	24,583	24,829	25,077	25,328	25,581
XLH Cases (adult)	17,026	17,197	17,369	17,542	17,718	17,895	18,074	18,255	18,437	18,621	18,808	18,996	19,186
KRN23 market share (adult)	3%	5%	10%	15%	18%	18%	18%	18%	18%	18%	18%	18%	9%
KRN23 patients (adult)	511	860	1,737	2,631	3,189	3,221	3,253	3,286	3,319	3,352	3,385	3,419	1,727
XLH Cases (ped)	5,675	5,732	5,790	5,847	5,906	5,965	6,025	6,085	6,146	6,207	6,269	6,332	6,395
KRN23 market share (ped)	5%	15%	25%	35%	45%	55%	65%	70%	70%	70%	70%	70%	40%
KRN23 patients (ped)	284	860	1,447	2,047	2,658	3,281	3,916	4,259	4,302	4,345	4,388	4,432	2,558
Price/patient/yr ('000)	85	85	85	85	85	85	85	85	85	85	85	85	85
EU KRN23 revenue ($M)	**67.6**	**146.2**	**270.6**	**397.6**	**497.0**	**552.7**	**609.4**	**641.3**	**647.8**	**654.2**	**660.7**	**667.3**	**364.2**
RARE EU Royalty (%)	*10%*	*10%*	*10%*	*10%*	*10%*	*10%*	*10%*	*10%*	*10%*	*10%*	*10%*	*10%*	*10%*
RARE EU Royalties	**6.8**	**14.6**	**27.1**	**39.8**	**49.7**	**55.3**	**60.9**	**64.1**	**64.8**	**65.4**	**66.1**	**66.7**	**36.4**
												122.145	
LATIN AMERICA (LATAM)													
LATAM population	623,249	629,481	635,776	642,134	648,555	655,041	661,591	668,207	674,889	681,638	688,455	695,339	702,293
XLH Cases	23,683	23,920	24,159	24,401	24,645	24,892	25,140	25,392	25,646	25,902	26,161	26,423	26,687
XLH Cases (adult)	17,763	17,940	18,120	18,301	18,484	18,669	18,855	19,044	19,234	19,427	19,621	19,817	20,015
KRN23 market share (adult)	1%	2%	3%	3%	3%	3%	3%	3%	3%	3%	3%	3%	1%
KRN23 patients (adult)	178	359	544	549	555	560	566	571	577	583	589	595	200
XLH Cases (ped)	5,921	5,980	6,040	6,100	6,161	6,223	6,285	6,348	6,411	6,476	6,540	6,606	6,672
KRN23 market share (ped)	1%	3%	6%	10%	15%	20%	20%	20%	20%	20%	20%	20%	10%
KRN23 patients (ped)	59	179	362	610	924	1245	1257	1270	1282	1295	1308	1321	667
Price/patient/yr ('000)	85	85	85	85	85	85	85	85	85	85	85	85	85
LATAM KRN23 sales ($M)	**20.1**	**45.7**	**77.0**	**98.5**	**125.7**	**153.4**	**155.0**	**156.5**	**158.0**	**159.6**	**161.2**	**162.9**	**73.7**
LATAM KRN23 revenues - less royalties($M)	**19.7**	**44.8**	**75.5**	**96.5**	**123.2**	**150.4**	**151.9**	**153.4**	**154.9**	**156.4**	**158.0**	**159.6**	**72.2**
WW KRN23 Revenues to RARE ($M)	**38.7**	**86.5**	**154.2**	**214.5**	**273.6**	**320.9**	**343.8**	**359.5**	**367.3**	**375.5**	**383.9**	**392.6**	**202.1**
WW KRN23 Revenues to RARE (prob adj, $M)	**29.0**	**64.9**	**115.7**	**160.9**	**205.2**	**240.7**	**257.8**	**269.6**	**275.5**	**281.7**	**288.0**	**294.5**	**151.6**

Source: Jefferies

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Exhibit 41: THN for LC-FAOD Market Model

	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E
US													
FAOD Cases	3,363	3,397	3,431	3,465	3,500	3,535	3,570	3,606	3,642	3,678	3,715	3,752	3,790
THN market share	10%	25%	40%	55%	60%	60%	60%	60%	30%	15%	8%	4%	2%
THN patients	336	849	1,372	1,906	2,100	2,121	2,142	2,164	1,093	552	279	141	71
Price/patient/yr ('000)	85	88	90	93	96	99	101	105	108	111	114	118	121
US THN revenue ($M)	**28.6**	**74.3**	**123.7**	**177.0**	**200.9**	**209.0**	**217.4**	**226.2**	**117.7**	**61.2**	**31.9**	**16.6**	**8.6**
EU													
FAOD Cases	5,045	5,095	5,146	5,198	5,250	5,302	5,355	5,409	5,463	5,517	5,573	5,628	5,685
THN market share	9%	20%	30%	40%	40%	40%	40%	40%	40%	40%	13%	7%	3%
THN patients	472	1,019	1,544	2,079	2,100	2,121	2,142	2,164	2,185	2,207	743	375	189
Price/patient/yr ('000)	85	85	85	85	85	85	85	85	85	85	85	85	85
EU THN revenue ($M)	**40.1**	**86.6**	**131.2**	**176.7**	**178.5**	**180.3**	**182.1**	**183.9**	**185.7**	**187.6**	**63.2**	**31.9**	**16.1**
ROW													
ROW population	757,357	764,930	772,580	780,305	788,109	795,990	803,949	811,989	820,109	828,310	836,593	844,959	853,409
FAOD Cases	6,059	6,119	6,181	6,242	6,305	6,368	6,432	6,496	6,561	6,626	6,693	6,760	6,827
THN market share	1%	3%	6%	10%	15%	15%	15%	15%	15%	15%	8%	4%	2%
THN patients	61	184	371	624	946	955	965	974	984	994	502	253	128
Price/patient/yr ('000)	85	85	85	85	85	85	85	85	85	85	85	85	85
ROW THN revenue ($M)	**5.2**	**15.6**	**31.5**	**53.0**	**80.4**	**81.2**	**82.0**	**82.8**	**83.6**	**84.5**	**42.7**	**21.5**	**10.9**
WW THN revenues ($M)	**73.9**	**176.6**	**286.5**	**406.8**	**459.8**	**470.5**	**481.5**	**493.0**	**387.1**	**333.3**	**137.7**	**70.0**	**35.5**
WW THN revenues (less royalties, $M)	**70.2**	**167.8**	**272.2**	**386.4**	**436.8**	**446.9**	**457.4**	**468.3**	**367.7**	**316.6**	**130.8**	**66.5**	**33.8**
WW THN revenues (prob adj, $M)	**49.1**	**117.4**	**190.5**	**270.5**	**305.8**	**312.9**	**320.2**	**327.8**	**257.4**	**221.6**	**91.6**	**46.5**	**23.6**

Source: Jefferies

Exhibit 42: THN for GLUT1 DS Market Model

	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E
US													
GLUT1 DS Cases	5,045	5,095	5,146	5,198	5,250	5,302	5,355	5,409	5,463	5,517	5,573	5,628	5,685
THN market share	10%	20%	30%	35%	40%	40%	40%	40%	13%	4%	2%	1%	1%
THN patients	504	1,019	1,544	1,819	2,100	2,121	2,142	2,164	728	245	124	63	32
Price/patient/yr ('000)	85	88	90	93	96	99	101	105	108	111	114	118	121
US THN revenue ($M)	**42.8**	**89.2**	**139.2**	**169.0**	**200.9**	**209.0**	**217.4**	**226.2**	**78.4**	**27.2**	**14.2**	**7.4**	**3.9**
EU													
GLUT1 DS Cases	7,567	7,643	7,719	7,797	7,875	7,953	8,033	8,113	8,194	8,276	8,359	8,443	8,527
THN market share	5%	13%	25%	35%	40%	40%	40%	40%	40%	40%	40%	20%	10%
THN patients	378	994	1,930	2,729	3,150	3,181	3,213	3,245	3,278	3,310	3,344	1,689	853
Price/patient/yr ('000)	85	85	85	85	85	85	85	85	85	85	85	85	85
EU THN revenue ($M)	**32.1**	**84.5**	**164.1**	**232.0**	**267.8**	**270.4**	**273.1**	**275.8**	**278.6**	**281.4**	**284.2**	**143.6**	**72.5**
ROW													
ROW population	757,357	764,930	772,580	780,305	788,109	795,990	803,949	811,989	820,109	828,310	836,593	844,959	853,409
GLUT1 DS Cases	9,846	9,944	10,044	10,144	10,245	10,348	10,451	10,556	10,661	10,768	10,876	10,984	11,094
THN market share	1%	3%	6%	10%	15%	15%	15%	15%	15%	15%	10%	5%	2%
THN patients	98	298	603	1,014	1,537	1,552	1,568	1,583	1,599	1,615	1,088	549	185
Price/patient/yr ('000)	85	85	85	85	85	85	85	85	85	85	85	85	85
ROW THN revenue ($M)	**8.3**	**25.3**	**51.3**	**86.2**	**130.6**	**131.9**	**133.3**	**134.6**	**135.9**	**137.3**	**92.5**	**46.7**	**15.7**
WW THN revenues ($M)	**83.3**	**199.0**	**354.5**	**487.1**	**599.3**	**611.3**	**623.8**	**636.6**	**492.9**	**445.8**	**390.9**	**197.6**	**92.1**
WW THN revenues (less royalties, $M)	**79.1**	**189.1**	**336.8**	**462.8**	**569.3**	**580.7**	**592.6**	**604.8**	**468.3**	**423.5**	**371.3**	**187.8**	**87.5**
WW THN revenues (Prob. Adj., $M)	**47.5**	**113.4**	**202.1**	**277.7**	**341.6**	**348.4**	**355.6**	**362.9**	**281.0**	**254.1**	**222.8**	**112.7**	**52.5**

Source: Jefferies

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Exhibit 43: rhGUS for MPS VII Market Model

	2017E	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E
US														
MPS VII Cases	94	95	95	96	97	98	99	100	101	102	103	104	104	105
rhGUS market share	10%	20%	40%	60%	70%	80%	80%	80%	80%	80%	80%	40%	20%	10%
# rhGUS patients	9	19	38	58	68	78	79	80	81	82	82	42	21	11
Price/patient/yr ('000)	450	450	450	450	450	450	450	450	450	450	450	450	450	450
US rhGUS revenue excluding royalty ($M)	**4.1**	**8.6**	**17.1**	**26.1**	**30.6**	**35.1**	**35.6**	**36.0**	**36.5**	**36.9**	**36.9**	**18.9**	**9.5**	**5.0**
EU														
MPS VII Cases	114	115	117	118	119	120	121	122	123	124	125	126	128	129
rhGUS market share	5%	10%	20%	35%	50%	60%	70%	70%	70%	70%	70%	23%	8%	3%
# rhGUS patients	6	12	23	41	60	72	85	85	86	87	88	29	10	3
Price/patient/yr ('000)	450	450	450	450	450	450	450	450	450	450	450	450	450	450
EU rhGUS revenue excluding royalty ($M)	**2.7**	**5.4**	**10.4**	**18.5**	**27.0**	**32.4**	**38.3**	**38.3**	**38.7**	**39.2**	**39.6**	**13.1**	**4.5**	**1.4**
ROW														
ROW population	749,858	757,357	764,930	772,580	780,305	788,109	795,990	803,949	811,989	820,109	828,310	836,593	844,959	853,409
MPS VII Cases	82	83	84	85	86	87	88	88	89	90	91	92	93	94
rhGUS market share	1%	3%	5%	7%	10%	15%	15%	15%	15%	15%	15%	5%	2%	1%
# rhGUS patients	1	2	4	6	9	13	13	13	13	14	14	5	2	1
Price/patient/yr ('000)	450	450	450	450	450	450	450	450	450	450	450	450	450	450
ROW rhGUS revenue excluding royalty ($M)	**0.5**	**0.9**	**1.8**	**2.7**	**4.1**	**5.9**	**5.9**	**5.9**	**5.9**	**6.3**	**6.3**	**2.3**	**0.9**	**0.5**
WW rhGUS revenues ($M)	**7.2**	**14.9**	**29.3**	**47.3**	**61.7**	**73.4**	**79.7**	**80.1**	**81.0**	**82.4**	**82.8**	**34.2**	**14.9**	**6.8**
WW rhGUS revenues (less royalties, $M)	**7.1**	**14.6**	**28.7**	**46.3**	**60.4**	**71.9**	**78.1**	**78.5**	**79.4**	**80.7**	**81.1**	**33.5**	**14.6**	**6.6**
WW rhGUS revenues (prob. Adj., $M)	**4.9**	**10.2**	**20.1**	**32.4**	**42.3**	**50.3**	**54.6**	**54.9**	**55.6**	**56.5**	**56.8**	**23.5**	**10.2**	**4.6**

Source: Jefferies

Exhibit 44: SA-ER for HIBM Market Model

	2018E	2019E	2020E	2021E	2022E	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E
US													
HIBM Cases	709	716	724	731	738	745	753	761	768	776	783	791	799
SA-ER market share	15%	30%	45%	60%	65%	65%	65%	65%	22%	7%	2%	1%	0%
SA-ER patients	106	215	326	439	480	484	489	495	166	56	19	6	2
Price/patient/yr ('000)	88	90	92	94	96	98	99	101	103	106	108	110	112
US SA-ER revenue ($M)	**9.4**	**19.4**	**30.0**	**41.1**	**45.9**	**47.2**	**48.6**	**50.2**	**17.2**	**5.9**	**2.0**	**0.7**	**0.2**
EU													
HIBM Cases	867	876	884	893	902	911	920	929	939	948	958	967	977
SA-ER market share	0%	15%	29%	44%	55%	60%	60%	60%	60%	60%	60%	20%	7%
SA-ER patients	0	128	259	393	496	547	552	557	563	569	575	193	65
Price/patient/yr ('000)	80	80	80	80	80	80	80	80	80	80	80	80	80
EU SA-ER revenue ($M)	**0.0**	**10.2**	**20.7**	**31.4**	**39.7**	**43.8**	**44.2**	**44.6**	**45.0**	**45.5**	**46.0**	**15.4**	**5.2**
ROW (Exc. Japan)													
ROW population	623,248	629,480	635,775	642,133	648,554	655,040	661,590	668,206	674,888	681,637	688,453	695,338	702,291
HIBM Cases	686	692	699	706	713	721	728	735	742	750	757	765	773
SA-ER market share	0%	1%	3%	5%	7%	10%	10%	10%	10%	10%	10%	3%	1%
SA-ER patients	0	7	21	35	50	72	73	74	74	75	76	26	9
Price/patient/yr ('000)	80	80	80	80	80	80	80	80	80	80	80	80	80
ROW SA-ER revenue ($M)	**0.0**	**0.6**	**1.7**	**2.8**	**4.0**	**5.8**	**5.8**	**5.9**	**5.9**	**6.0**	**6.1**	**2.1**	**0.7**
WW SA-ER revenues ($M)	**9.4**	**30.2**	**52.4**	**75.4**	**89.6**	**96.7**	**98.6**	**100.7**	**68.1**	**57.4**	**54.1**	**18.2**	**6.1**
WW SA-ER revenues (less royalties, $M)	**8.6**	**27.8**	**48.2**	**69.4**	**82.4**	**89.0**	**90.7**	**92.6**	**62.7**	**52.8**	**49.8**	**16.7**	**5.7**
WW SA-ER revenues (prob adj., $M)	**6.0**	**19.4**	**33.7**	**48.6**	**57.7**	**62.3**	**63.5**	**64.9**	**43.9**	**37.0**	**34.9**	**11.7**	**4.0**

Source: Jefferies

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Company Description

Ultragenyx Pharmaceutical, Inc. is a clinical-stage biotechnology company. The company is focused on the identification, acquisition, development, and commercialization of novel products for the treatment of rare and ultra-rare diseases, with an initial focus on serious, debilitating metabolic genetic diseases. Ultragenyx Pharmaceutical was founded by Emil D. Kakkis on April 22, 2010 and is headquartered in Novato, CA.

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- BioMarin Pharmaceutical Inc. (BMRN: $69.08, BUY)
- Sangamo Biosciences, Inc. (SGMO: $10.77, BUY)
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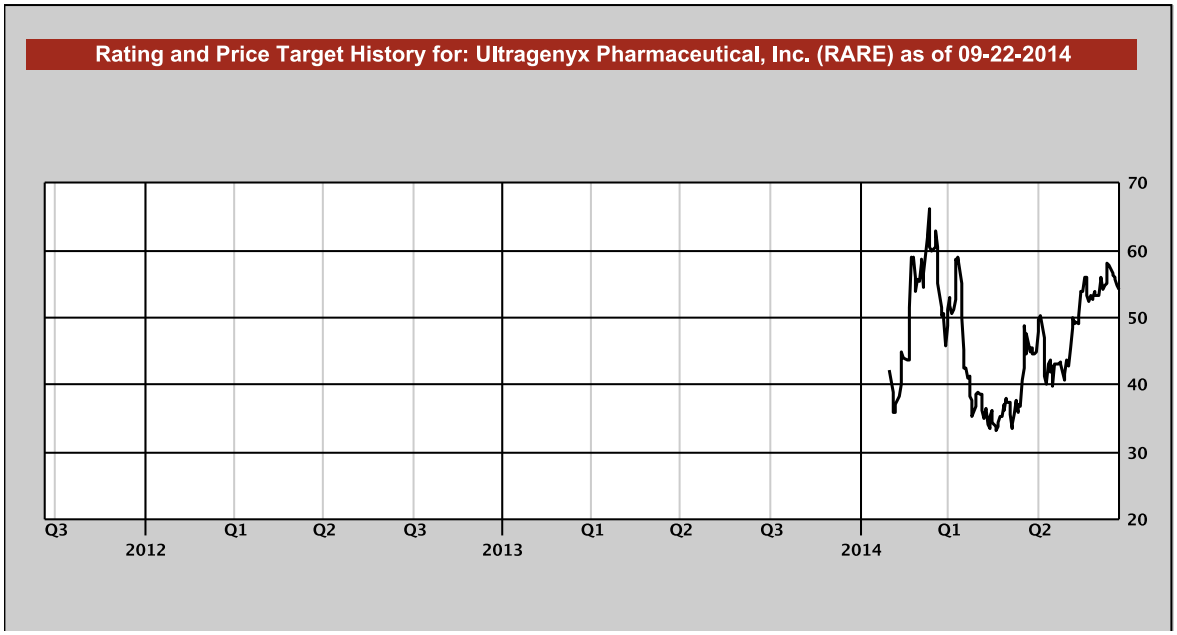

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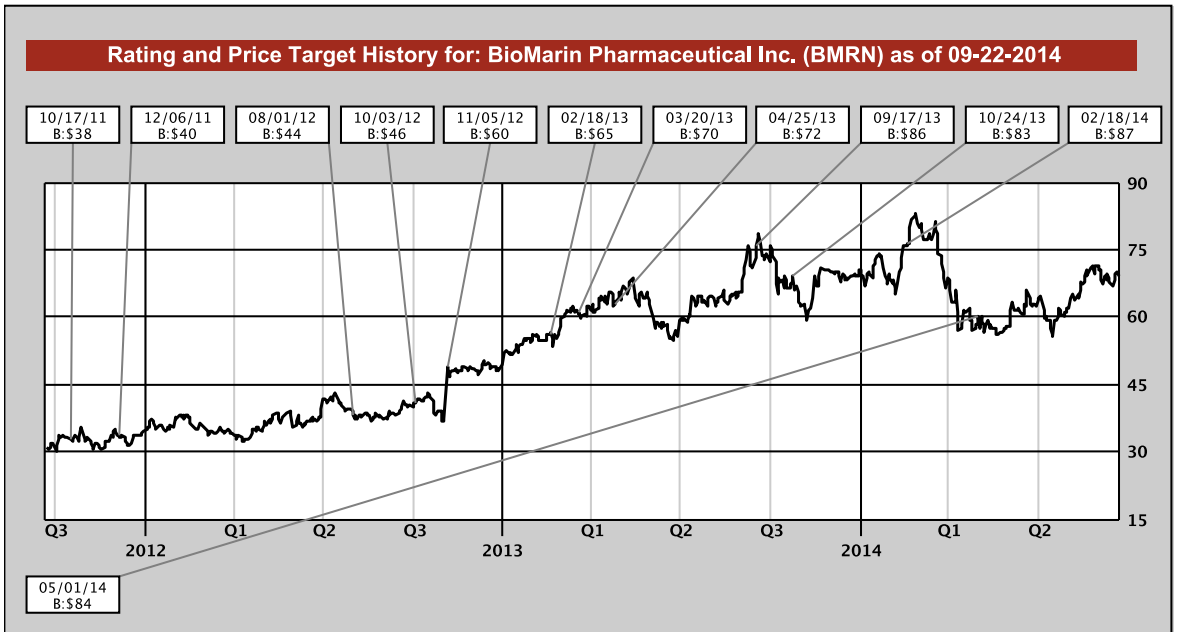

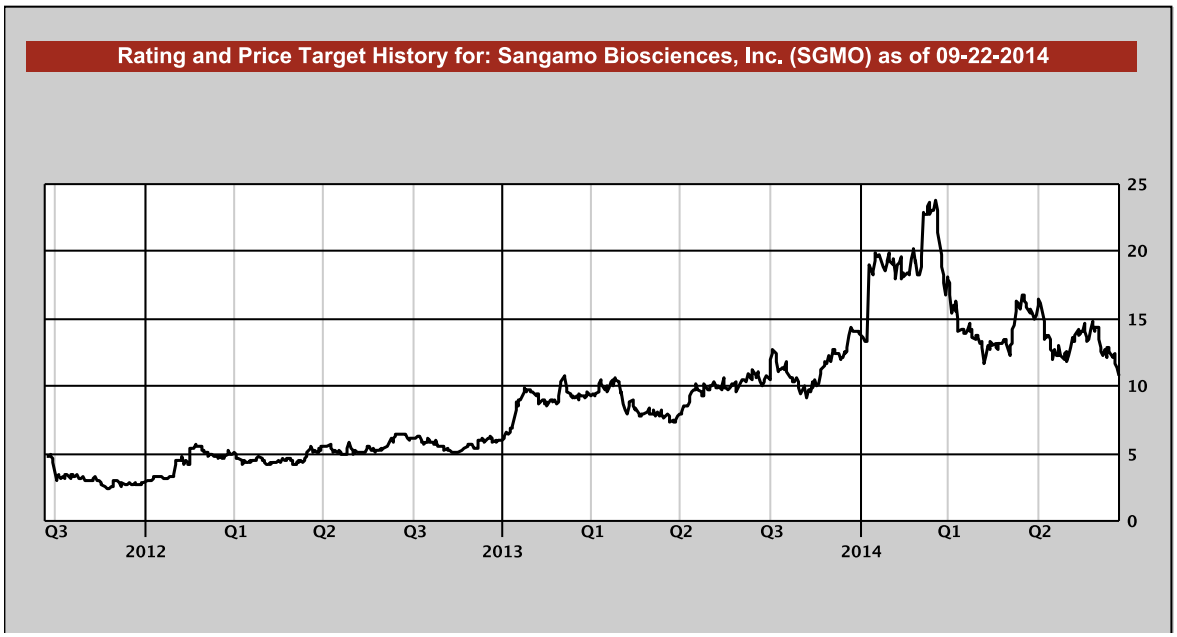

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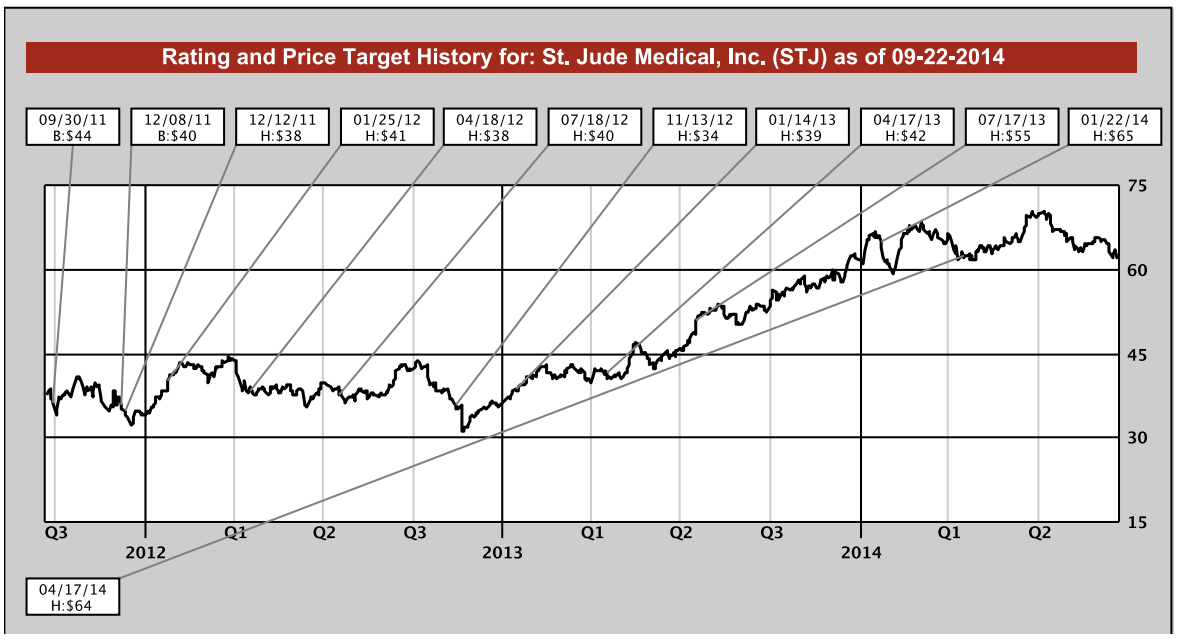

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