Ultragenyx

Equity Research

Company Quick Take

December 30, 2014

Price: $44.06 (12/26/2014)
Price Target: NA

OUTPERFORM (1)

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Key Data

Symbol	NASDAQ: RARE
Market Cap (MM)	$1,405.5

KRN23: More Than Just XLH

The Cowen Insight

Ultragenyx recently initiated a trial of KRN23 (anti-FGF23 mAb) in ENS and TIO. This is the first expansion of KRN23 beyond the XLH market (sales modeled as >$1.4B WW). We believe ENS, TIO and other disorders of FGF23 overproduction (e.g. ADHR, ARHR) could support $650MM+ in upside to KRN23 sales estimates. With multiple data readouts in 2015, Ultragenyx remains a top pick.

FGF23 Plays A Role In Diseases Beyond XLH

Ultragenyx's clinical pipeline features four late-stage candidates in development for multiple orphan disorders. The company's most prominent candidate is KRN23, an anti-FGF23 antibody being developed in partnership with Kyowa Hakko Kirin. FGF23 is a hormonal regulator of phosphate metabolism that is overexpressed in the genetic disorder X-linked hypophosphatemia (XLH), the drug's lead indication. It is well established that patients with XLH have elevated levels of FGF23 that cause the kidney to excrete excessive amounts of phosphate, leading to hypophosphatemia, and ultimately rickets and other clinical abnormalities. We model 3,000 pediatric and 9,000 adult XLH patients in the U.S. with similar numbers ex-U.S. Based upon an initial annual price of $50K/yr, we believe XLH could ultimately support >$600MM in peak U.S. XLH sales and >$1.4B in worldwide sales. We model Ultragenyx receiving revenue in excess of $400MM in this indication.

It is increasingly recognized that FGF23 plays a central role in regulating phosphate metabolism, and that the disregulation of FGF23 may lie at the root of other hypophosphatemic disorders. As a result, KRN23 may also have a role treating diseases like autosomal dominant hypophosphatemic rickets (ADHR), autosomal recessive hypophosphatemic rickets (ARHR), epidermal nevus syndrome (ENS) and tumor-induced osteomalacia (TIO). We believe investors are largely unaware of these opportunities. In fact, Ultragenyx has recently opened a single-center Phase II trial of KRN23 in TIO and ENS. Below we discuss each of these disorders and the potential market opportunity for KRN23.

Autosomal Dominant Hypophosphatemic Rickets

ADHR is caused by mutations in the FGF23 gene. These mutations lead to stabilization of circulating FGF23. As cells in the bone (osteoclasts) secrete FGF23, circulating FGF23 levels increase and remain above normal levels. Over time hypophosphatemia and ultimately rickets occurs. Consultants predict that if KRN23 works in XLH it will almost certainly work in ADHR given FGF23's central role in both diseases. They note that incidence data on ADHR are lacking, but estimate the presence of ADHR disease at ~1:100,000 individuals. Using this estimate of disease incidence and assuming ~60% market penetration, we estimate that ADHR has the potential for ~$325MM in peak WW sales, translating to a potential $112MM in revenue for Ultragenyx.

Autosomal Recessive Hypophosphatemic Rickets

Please see addendum of this report for important disclosures.

ARHR can be caused by mutations in multiple genes including dentin matrix protein 1 (DMP1) and ectonucleotide pyrophosphatase/phosphodiesterase 1 (ENPP1). DMP1 can function as an extracellular matrix protein involved in bone mineralization or as a nuclear protein that regulates the expression of a number of osteoblast genes including FGF23. Wild-type nuclear DMP1 suppresses FGF23 production. As a result, when DMP1 is mutated, control over FGF23 production is lost, and osteoclasts over excrete FGF23. As in other hypophosphatemic diseases, the resulting accumulation of serum FGF23 causes phosphate wasting and ultimately rickets. Wild-type ENPP1 plays a role in the production of inorganic pyrophosphate. However, the mechanism by which mutations in ENPP1 lead to excessive FGF23 production is unknown. Consultants report that there are additional less well characterized mutations that yield excessive FGF23 production and a similar ARHR disease phenotype. In total, they estimate that ARHR disease occurs in ~1:100,000 individuals. Hence as in ADHR, this might translate into an additional ~$325MM peak WW sales opportunity, or a potential $112MM in revenue for Ultragenyx.

Epidermal Nevus Syndrome and Tumor Induced Osteomalacia

ENS and TIO are diseases in which mutations within a lesion or tumor lead to FGF23 production in non-osteoclast cells. As in ADHR and ARHR, excessive FGF23 production results in the development of bone deformities, fractures, and/or rickets. In either ENS or TIO, removal of the tumor/lesion leads to a cure of the patient's hypophosphatemia. In ENS, lesions occur as an epidermal nevus which are generally abnormally pigmented and easily spotted. However, the location of the nevus (if it is on the face, for example) may restrict the ability to surgically remove the lesion. In TIO, the tumor may be very small in size and located anywhere within the body. Therefore, in some patients with TIO it may take months/years to locate the source of FGF23 overproduction. Ultragenyx has recently opened a Phase II trial of KRN23 in inoperable ENS/TIO patients. The trial will enroll 6 patients to receive KRN23 every four weeks for 44 weeks. Our consultants expressed strong confidence in KRN23's ability to reverse ENS/TIO's bone effects, but also report that these conditions are very rare and may amount to a few hundred patients in the U.S. We expect Ultragenyx to quantify the market opportunity for KRN23 in ENS and TIO in the near future.

Valuation Methodology And Risks

Valuation Methodology

Biotechnology:

In calculating our 12-month target price, we employ one or more valuation methodologies, which include a discounted earnings analysis, discounted cash flow analysis, net present value analysis and/or a comparable company analysis. These analyses may or may not require the use of objective measures such as price-to-earnings or price-to-sales multiples as well as subjective measures such as discount rates.

We make investment recommendations on early stage (pre-commercial) biotechnology companies based upon an assessment of their technology, the probability of pipeline success, and the potential market opportunity in the event of success. However, because these companies lack traditional financial metrics, we do not believe there are any good methodologies for assigning a specific target price to such stocks.

Investment Risks

Biotechnology:

There are multiple risks that are inherent with an investment in the biotechnology sector. Beyond systemic risk, there is also clinical, regulatory, and commercial risk. Additionally, biotechnology companies require significant amounts of capital in order to develop their clinical programs. The capital-raising environment is always changing and there is risk that necessary capital to complete development may not be readily available.

Risks To The Price Target

Investing in development stage biotechnology companies is risky, and many things could prevent Ultragenyx from achieving the success we model.

Addendum

Stocks Mentioned In Important Disclosures

Ticker	Company Name
RARE	Ultragenyx

Analyst Certification

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Outperform (1): The stock is expected to achieve a total positive return of at least 15% over the next 12 months

Market Perform (2): The stock is expected to have a total return that falls between the parameters of an Outperform and Underperform over the next 12 months

Underperform (3): Stock is expected to achieve a total negative return of at least 10% over the next 12 months

Assumption: The expected total return calculation includes anticipated dividend yield

Cowen and Company Rating System until May 25, 2013

Outperform (1): Stock expected to outperform the S&P 500

Neutral (2): Stock expected to perform in line with the S&P 500

Underperform (3): Stock expected to underperform the S&P 500

Assumptions: Time horizon is 12 months; S&P 500 is flat over forecast period

Cowen Securities, formerly known as Dahlman Rose & Company, Rating System until May 25, 2013

Buy – The fundamentals/valuations of the subject company are improving and the investment return is expected to be 5 to 15 percentage points higher than the general market return

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Cowen And Company Rating Definitions

Distribution of Ratings/Investment Banking Services (IB) as of 09/30/14

Rating	Count	Ratings Distribution	Count	IB Services/Past 12 Months
Buy (a)	440	59.95%	105	23.86%
Hold (b)	278	37.87%	10	3.60%
Sell (c)	16	2.18%	0	0.00%

(a) Corresponds to "Outperform" rated stocks as defined in Cowen and Company, LLC's rating definitions. (b) Corresponds to "Market Perform" as defined in Cowen and Company, LLC's ratings definitions. (c) Corresponds to "Underperform" as defined in Cowen and Company, LLC's ratings definitions.

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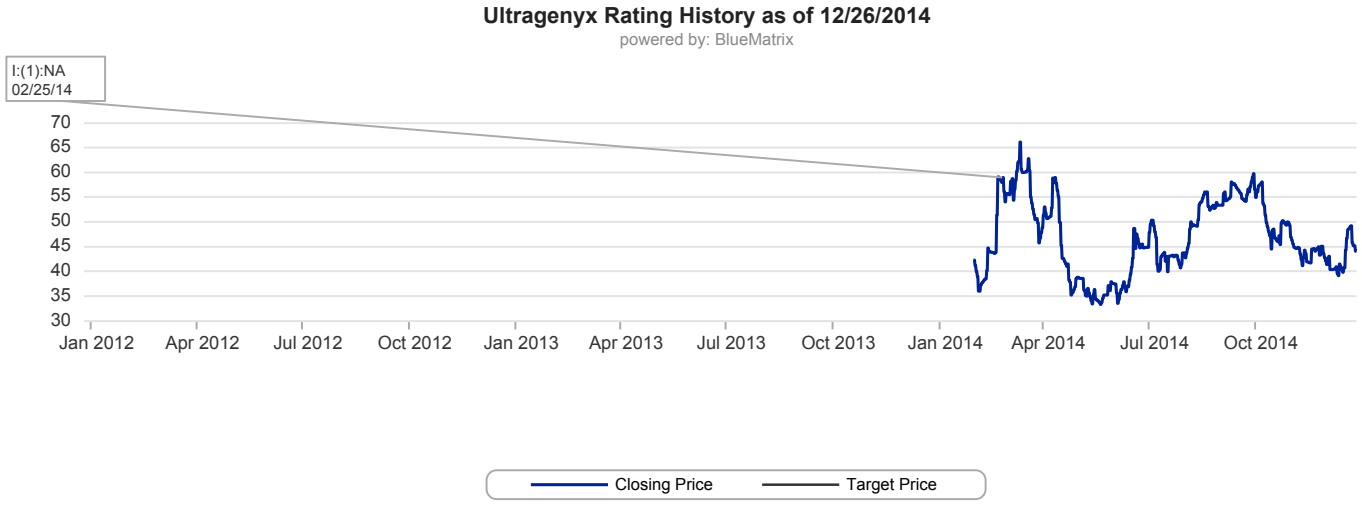

Legend for Price Chart:

I = Initiation | 1 = Outperform | 2 = Market Perform | 3 = Underperform | UR = Price Target Under Review | T = Terminated Coverage | $xx = Price Target | NA = Not Available | S=Suspended

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