COWEN
AND COMPANY

Biotechnology

Ultragenyx

Equity Research

Company Quick Take

December 16, 2014

Price: $39.76 (12/15/2014)

Price Target: NA

OUTPERFORM (1)

Eric Schmidt, Ph.D.
646.562.1345
eric.schmidt@cowen.com

Marc Frahm, Ph.D.
646.562.1394
marc.frahm@cowen.com

Key Data

Symbol	NASDAQ: RARE
Market Cap (MM)	$1,268.3

Laying The Groundwork For A Busy 2015

The Cowen Insight

Last week we hosted investor meetings with Ultragenyx's CEO Dr. Emil Kakkis and CFO Shalini Sharp. Ultragenyx is focused on creating value in orphan disorders by advancing a pipeline that features two Phase III and three Phase II programs. Limited H2:14 newsflow has been an overhang on shares, but 2015 promises to be a data rich year. RARE remains a top smid cap pick.

KRN23 Phase IIb Pediatric XLH Data Around Mid 15

KRN23 (fully human anti-FGF23 antibody) is in Phase II development for X-linked hypophosphatemia (XLH). XLH is a rare genetic disorder where bones produce excessive FGF23, causing the kidneys to excessively excrete phosphate, resulting in bone disease (rickets) and other abnormalities. In October, Ultragenyx announced that the open label Phase II trial had enrolled ~30 pediatric XLH patients. Following a 16 week titration period patients will receive KRN23 either every two or four weeks for 48 weeks. While the trial is not powered for a specific result, the key endpoints will be patient's radiographic rickets and growth scoring. Interim efficacy and safety data from the ongoing pediatric Phase II trial will be assessed following 24 weeks of stable therapy (scheduled for mid-2015). Based upon Alexion's experience with HPP, management believes that 24 weeks of therapy could be sufficient to see evidence of physiologic changes within a pediatric population. Management also suggested that there is a possibility the trial could be upsized to provide for a registration package as rickets and growth scoring are FDA approvable endpoints. However, the FDA has also indicated that approval will require data on the standard of care (SOC = Vitamin D + oral phosphate), which Ultragenyx believes could be provided either from a randomized Phase III trial (KRN23 vs. SOC) or a natural history study. SOC is traditionally dosed sub-optimally to reduce the risk of nephrocalcinosis, as a result management believes a randomized Phase III trial would be difficult to conduct. Therefore Ultragenyx is hoping a natural history study may be sufficient and plans to initiate such a trial in H1:15. An adult Phase IIb XLH trial is also scheduled to begin in H1:15. Adult bones turnover more slowly than pediatric bones, therefore management believes an important component of adult efficacy may be improvements in muscle function/mobility. Data from the pivotal adult trial is anticipated to support simultaneous approval in the pediatric and adult XLH settings. Given over 10,000 patients are believed to have XLH in the U.S., we believe KRN23 has $1-2B in peak potential, with RARE scheduled to receive about a third of its value from partner Kyowa Hakko Kirin.

rhGUS Phase III Trial Underway, Named Patient Sales Targeted For YE:15

Mucopolysaccharidosis 7 is a rare lysosomal storage disease characterized by a deficiency in beta-glucuronidase leading to an accumulation of glycosaminoglycans (GAG), enlarged liver/spleen, pulmonary disease, joint stiffness, and ultimately death at 10-30 years of age for most patients. Ultragenyx has completed a Phase I/II trial of rhGUS (recombinant human beta-glucuronidase) in three patients suffering from MPS7. Interim 12-week data from this trial indicates that doses of 1-4mg/kg

successfully lowered urinary GAG (uGAG). Full 36 week data is scheduled to be presented at the Lysosomal Disease Network's Annual World Symposium in February 2015.

Yesterday, Ultragenyx announced that is has begun enrolling a Phase III trial of rhGUS in MPS7. The trial will enroll 12 patients at U.S. Centers, all of which have already been identified, in a "blind start" design utilizing a 4mg/kg every other week dose. Patients will be randomized to one of four groups that will either begin rhGUS immediately or begin on placebo before transitioning to rhGUS at 8, 16, or 24 weeks. All patients will receive rhGUS for a minimum of 24 weeks and be followed for a total of 48 weeks. Patients will be assessed for improvements in uGAG, pulmonary function, walking, stair climb, shoulder flexion, fin and gross motor function, spleen/liver volume, cardiac volume/function, visual acuity, as well as caregiver and patient assessments. Ultragenyx has reached agreement with both the EMA and FDA on approval criteria for rhGUS. The EMA considers uGAG reductions sufficient for approval if supported by a trend toward improvement in what the EMA believes are the most important clinical endpoints (6MWT, FEV, spleen/liver size). The FDA will consider the totality of the uGAG and clinical endpoint data on a patient-by-patient basis. Management believes the pivotal MPS7 trial represents the smallest placebo-controlled pivotal trial in FDA history.

Management reports that it has already identified nearly 100 patients with MPS7. Based upon this experience and existing literature reports, Ultragenyx is very confident that there are at least 200 patients suffering from MPS7 in the developed world. In addition, Ultragenyx believes one reason for MPS7's apparent rarity among the MPS diseases is that it can present in a more severe hydrops form. Hydrops MPS7 usually leads to death within the first year of life. Management believes ~20 hydrops babies are born each year, and represent significant upside to the market potential of the traditional MPS7 presentation assuming the disease can be diagnosed and early mortality prevented. In fact, Ultragenyx is already treating one hydrops baby under an eIND. Finally, management believes the U.S. only design of the ongoing Phase III trial will allow Ultragenyx to pursue named patient sales in the EU and Turkey. These sales could begin as early as YE:15, approximately one year in advance of our model. Significantly, management described rhGUS production cultures as 10X more productive than other MPS programs. Therefore, MPS7 margins could exceed those found in other enzyme replacement therapies such as aldurazyme and naglazyme.

Triheptanoin Continues To Show Signs Of Efficacy In LC-FAOD, PIII Endpoint Needed

Ultragenyx is developing triheptanoin (a C7 triglyceride) for multiple indications including long-chain fatty acid oxidation disorders (FAOD). FAODs are caused by a constellation of mutations in the cellular machinery required to convert fatty acid into acetyl-CoA to feed the Krebs cycle. FAODs are believed to afflict 2,000-3,500 patients in the U.S. Triheptanoin is designed to circumvent the mutations by providing an alternative energy source. Ultragenyx is currently conducting a Phase II FAOD trial, which is "essentially" fully enrolled. For the primary analysis, approximately 30 patients will be treated for 24 weeks with triheptanoin. This initial treatment period will be followed by a 54-week extension period. Management reports that it is unaware of any prior clinical trials conducted in FAODs, and therefore that its Phase II design is hypothesis generating rather than hypothesis testing (i.e. designed to identify a valid Phase III endpoint). As a result, the trial will evaluate a host of endpoints including exercise tolerance (cycle ergometer/12MWT, muscle strength), hypoglycemic event rate, liver size, and cardiac disease. Importantly, it may be necessary to design a Phase III trial to match these endpoints to each patient's unique manifestations of FAOD (similar to the Phase III MPS7 agreement). Data from the initial 24-week

treatment period is expected around mid-2015. In addition to the ongoing clinical trial, management is providing triheptanoin on a compassionate use basis. Requests have been strong, particularly amongst patients suffering from heart failure as a result of FAOD. Management reports that these patients are generally extremely difficult to treat. However, of the nine patients treated so far, six have resolved their cardiomyopathy and two have stabilized.

Triheptanoin In Glut1 DS Phase II Trial To Include Absence Seizures

Glut1 deficiency syndrome (Glut1 DS) is a disease characterized by deficiencies in the glucose transporter responsible for moving glucose across the blood brain barrier. Lack of glucose in the brain, starves the brain leading to seizures, movement disorders, and developmental delays. Glut1 DS patients are currently treated with a ketogenic diet that is only modestly effective at reducing seizures. Triheptanoin is known to cross the blood brain barrier, and Ultragenyx is conducting a 50-patient placebo controlled Phase II trial. The trial is powered to detect a 40-50% reduction in seizures, with additional assessments of movement disorders and developmental delays. Management reports that patients are ineligible for the trial if they are being treated with a ketogenic diet and this has led to slow enrollment. As a result, Ultragenyx is in the process of amending the trial to allow patients with absence seizures (often Glut1 derived) to enroll. With this amendment, Ultragenyx is hopeful that data will be available in H2:15.

SA-ER Phase III Moving Forward

Hereditary Inclusion Body Myopathy (HIBM) is a rare myopathy believed to occur as a result of mutations that deprive cells of sialic acid required for protein sialization and function. Ultragenyx has previously guided to an incidence of 1,200-2,000 patients in the developed world. However, a recent genetic publication suggests the incidence could be 3X larger. In addition, management has already generated a database of 1,200 identified HIBM patients. Ultragenyx is developing an extended release formulation of sialic acid (SA-ER) for these patients. A Phase II trial of 3, 6, and 12g (6g of SA-ER+6g of immediate release SA) has generated positive data in patients with a baseline 6MWT >20m. This trial has demonstrated significant preservation of upper extremity muscle strength in the 6g group relative to either placebo (+5.5%; p=0.040) at 24 weeks or 3g (+8.5%; p=0.0033) of SA-ER at 48 weeks. Importantly, the upper extremity effect using 6g was strongest among patients with a baseline 6MWT of >200m (+9.6%; p=0.00055). Unfortunately, strength preservation was not observed in lower extremities and a 12g trial extension did not further improve efficacy across the population. Nonetheless, management reports that some patients "clearly" benefited from higher doses and will be kept on the 12g dose during extension trials. In mid-2015, management intends to initiate a Phase III trial using the 6g dose in ~80 HIBM patients with 6MWT tests >200m. Patients will be treated for one year. Importantly, the FDA has accepted Ultragenyx's primary endpoint of upper extremity muscle strength instead of the traditional muscle disorder endpoint of 6MWT. The ability to measure efficacy on upper extremity rather than lower extremity muscles is a first. This reiterates Ultragenyx's differentiated ability to work with the FDA to develop the novel clinical trial designs required to bring orphan drugs to market.

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

Each author of this research report hereby certifies that (i) the views expressed in the research report accurately reflect his or her personal views about any and all of the subject securities or issuers, and (ii) no part of his or her compensation was, is, or will be related, directly or indirectly, to the specific recommendations or views expressed in this report.

Important Disclosures

Cowen and Company, LLC and or its affiliates make a market in the stock of Ultragenyx securities.

Ultragenyx has been client(s) of Cowen and Company, LLC in the past 12 months.

Ultragenyx is or was in the past 12 months a client of Cowen and Company, LLC; during the past 12 months, Cowen and Company, LLC provided IB services.

Cowen and Company, LLC and/or its affiliates received in the past 12 months compensation for investment banking services from Ultragenyx.

Cowen and Company, LLC and/or its affiliates managed or co-managed a public offering of Ultragenyx within the past twelve months.

Cowen and Company, LLC compensates research analysts for activities and services intended to benefit the firm's investor clients. Individual compensation determinations for research analysts, including the author(s) of this report, are based on a variety of factors, including the overall profitability of the firm and the total revenue derived from all sources, including revenues from investment banking. Cowen and Company, LLC does not compensate research analysts based on specific investment banking transactions.

Disclaimer

This research is for our clients only. Our research is disseminated primarily electronically and, in some cases, in printed form. Research distributed electronically is available simultaneously to all Cowen and Company, LLC clients. All published research can be obtained on the Firm's client website, https://cowenlibrary.bluematrix.com/client/library.jsp.

Further information on any of the above securities may be obtained from our offices. This report is published solely for information purposes, and is not to be construed as an offer to sell or the solicitation of an offer to buy any security in any state where such an offer or solicitation would be illegal. Other than disclosures relating to Cowen and Company, LLC, the information herein is based on sources we believe to be reliable but is not guaranteed by us and does not purport to be a complete statement or summary of the available data. Any opinions expressed herein are statements of our judgment on this date and are subject to change without notice.

For important disclosures regarding the companies that are the subject of this research report, please contact Compliance Department, Cowen and Company, LLC, 599 Lexington Avenue, 20th Floor, New York, NY 10022. In addition, the same important disclosures, with the exception of the valuation methods and risks, are available on the Firm's disclosure website at https://cowen.bluematrix.com/sellside/Disclosures.action.

Price Targets: Cowen and Company, LLC assigns price targets on all covered companies unless noted otherwise. The price target for an issuer's stock represents the value that the analyst reasonably expects the stock to reach over a performance period of twelve months. The price targets in this report should be considered in the context of all prior published Cowen and Company, LLC research reports (including the disclosures in any such report or on the Firm's disclosure website), which may or may not include price targets, as well as developments relating to the issuer, its industry and the financial markets. For price target valuation methodology and risks associated with the achievement of any given price target, please see the analyst's research report publishing such targets.

Notice to UK Investors: This publication is produced by Cowen and Company, LLC which is regulated in the United States by FINRA. It is to be communicated only to persons of a kind described in Articles 19 and 49 of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005. It must not be further transmitted to any other person without our consent.

Cowen and Company, LLC. New York (646) 562-1000 **Boston** (617) 946-3700 **San Francisco** (415) 646-7200 **Chicago** (312) 577-2240 **Cleveland** (440) 331-3531 **Atlanta** (866) 544-7009 **London** (affiliate) 44-207-071-7500

COWEN AND COMPANY RATING DEFINITIONS

Cowen and Company Rating System effective May 25, 2013

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

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

Hold – The fundamentals/valuations of the subject company are neither improving nor deteriorating and the investment return is expected to be in line with the general market return

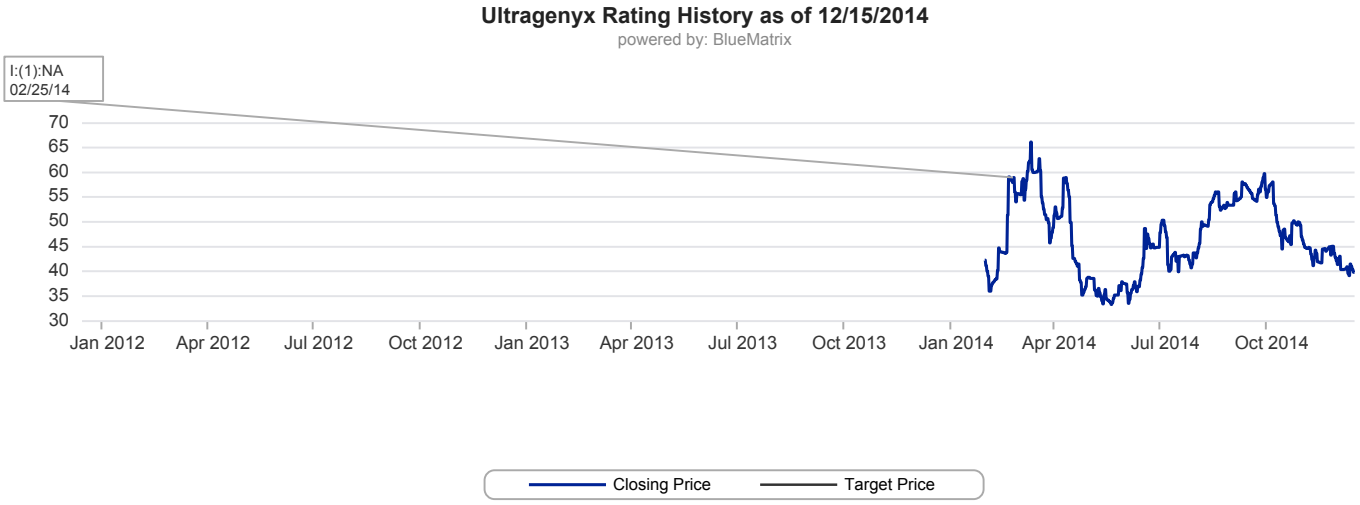
Cowen And Company Rating Definitions

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.

Note: "Buy", "Hold" and "Sell" are not terms that Cowen and Company, LLC uses in its ratings system and should not be construed as investment options. Rather, these ratings terms are used illustratively to comply with FINRA and NYSE regulations.



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

Points Of Contact

Reaching Cowen

Main U.S. Locations

New York
599 Lexington Avenue
New York, NY 10022
646.562.1000
800.221.5616

Boston
Two International Place
Boston, MA 02110
617.946.3700
800.343.7068

Cleveland
20006 Detroit Road
Suite 100
Rocky River, OH 44116
440.331.3531

San Francisco
555 California Street, 5th Floor
San Francisco, CA 94104
415.646.7200
800.858.9316

Atlanta
3399 Peachtree Road NE
Suite 417
Atlanta, GA 30326
866.544.7009

Chicago
181 West Madison Street
Suite 1925
Chicago, IL 60602
312.577.2240

International Locations

Cowen International Limited

London
1 Snowden Street - 11th Floor
London EC2A 2DQ
United Kingdom
44.20.7071.7500

Cowen and Company (Asia) Limited

Hong Kong
Suite 1401 Henley Building
No. 5 Queens Road Central
Central, Hong Kong
852 3752 2333