

Today's Changes	Annual EPS	Annual Revenue	Target
	No change	No change	\$30.00 from \$26.00

Radius Health

RDUS : NASDAQ : US\$23.11

BUY**Target: US\$30.00 ↑**

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COMPANY STATISTICS:

Forecast Return:	29.8%
Shares Out (M):	26.0
Market Cap (M):	US\$599.7
52-week Range:	7.46 - 24.28
Avg. Daily Vol. (000s):	110.5

EARNINGS SUMMARY:

FYE Dec	2013A	2014E	2015E	2016E
Revenue (M):	0.0	0.0	0.0	82.1
EPS:	(3.97)	(54.39)	(2.78)	(1.53)

Revenue (M):	Q1	0.0	0.0A	0.0	-
	Q2	0.0	0.0A	0.0	-
	Q3	0.0	0.0	0.0	-
	Q4	0.0	0.0	0.0	-
	Total	0.0	0.0	0.0	82.1
EPS:	Q1		(50.45)A	(0.70)A	-
	Q2		(2.22)A	(0.77)A	-
	Q3	0.00	(0.88)	(0.69)	-
	Q4	0.00	(0.84)	(0.62)	-
	Total	(3.97)	(54.39)	(2.78)	(1.53)

SHARE PRICE PERFORMANCE:



Source: Interactive Data Corporation

COMPANY DESCRIPTION:

Radius is a biotechnology company focused on discovering, developing, and commercializing drugs for endocrine disorders. Its wholly owned lead asset is abaloparatide, in Phase 3 for treatment of postmenopausal osteoporosis.

All amounts in US\$ unless otherwise noted.

Life Sciences -- Biotechnology

RAD1901 EARLY, BUT INTERESTING FOR BRAIN METASTASES

Investment highlights

\$1.7B Seragon acquisition advantageous to RAD1901

Roche's recent ~\$1.7B acquisition of Seragon for its early-stage SERD (ARN-810) suggests healthy interest in the SERD area, including RAD1901. We also believe RAD1901's potential to cross the blood brain barrier could be an advantage vs. current therapies. Additionally, RAD1901 may avoid the uterine cancer and bone loss risk associated with AIs or tamoxifen, possibly permitting RAD1901 to earlier treatment settings in hormone receptor positive metastatic breast cancer (MBC).

RAD1901 early, but could address ~\$1.4B market in MBC

Analysis shows RAD1901 has potential to penetrate the ~\$850M hormone receptor positive MBC population and ~\$540M MBC + brain metastases market. We do not include RAD1901 in our valuation given its early stage, but believe continued positive data could contribute to long-term upside for RDUS.

Recent Phase I update at EORTC conference promising

New highlights from the Phase I MTD trial for RAD1901 showed suppression of ER signals via PET scans after only six days of dosing, a move forward towards initiating a 1b clinical trial, possibly starting YE14. We expect top-line data from the Phase I MTD trial YE14 at SABCS and results from the 1b trial in MBC presented at ASCO in 2015.

Raising price target to \$30 from \$26

We are raising our price target to \$30 from \$26 given prior market expansion for injectable non-bisphosphonate drugs. We believe abaloparatide will have better efficacy data compared to Forteo, which could expand the market. We are raising our US peak sales estimate to ~\$820M vs. ~\$650M previously.

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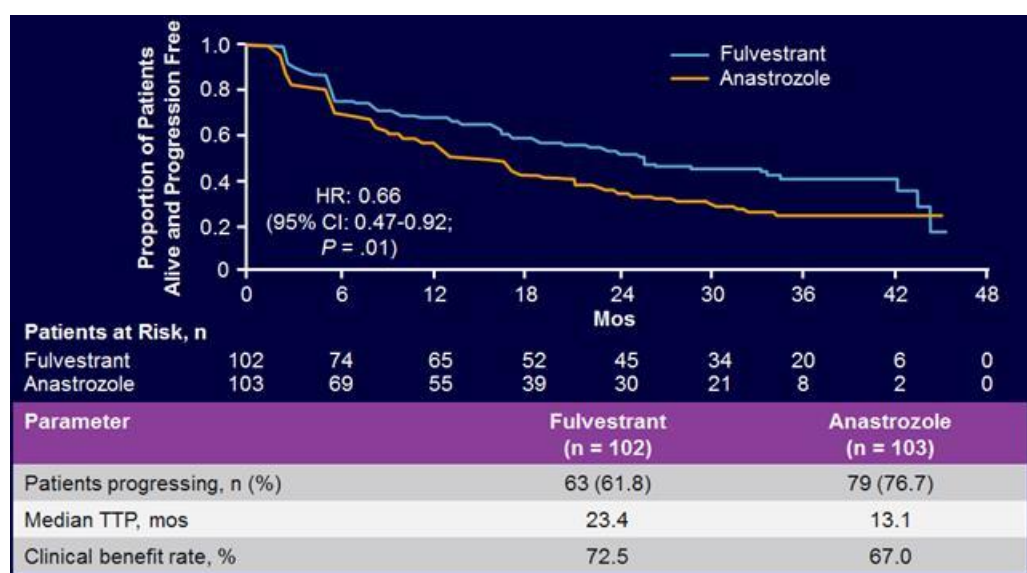
The recommendations and opinions expressed in this research report accurately reflect the Investment Analyst's personal, independent and objective views about any and all the Designated Investments and Relevant Issuers discussed herein. For important information, please see the Important Disclosures section in the appendix of this document.

DUAL COMPETITION OF ESTROGEN RECEPTOR WITH SERDS

The estrogen receptor alpha (ER α) is expressed in the majority of breast tumors, enabling therapeutic interventions targeting ER activity at the level of receptor activation (tamoxifen) or ligand synthesis (aromatase inhibitors). These approaches can have a dramatic positive impact on tumor proliferation. Even though resistance eventually develops to these agents over time or de novo, the ER α target continues to be important. This paradoxical finding is due to the hyperactivation of signaling pathways that can result in ligand independent transcriptional activation of the receptor. Therefore, it is no surprise that Selective Estrogen Receptor Degraders (SERDs) may be especially helpful in patients failing initial hormones with tamoxifen/aromatase inhibitors. Currently, the only approved SERD for clinical use is fulvestrant, demonstrating a complete antagonist/inverse agonist of ER α activity.

In the FIRST trial, patients with previously untreated HR+ advanced BC were randomized to fulvestrant 500 mg days 0, 14, 28, and every 28 days thereafter vs. anastrozole 1 mg daily. Secondary analysis showed significant increased time to progression with fulvestrant vs. anastrozole, with a hazard ratio of 0.66 (95% CI: 0.47 – 0.92). Median time to progression was 23.4 months with fulvestrant vs. 13.1 months in the anastrozole arm (Robertson JFR et al, SABCS 2010). These results reflect the benefit of fulvestrant 500 mg vs. anastrozole as front-line endocrine therapy for HR+ advanced BC in terms of time to progression, with a 34% reduction in risk of progression (P=0.01).

Figure 1: Secondary analysis from FIRST trial – fulvestrant vs. anastrozole



Source: Robertson JFR et al. SABCS 2010

However, fulvestrant has poor pharmacological/pharmaceutical properties, requiring a two time monthly intramuscular injection. Additionally, long term treatment with fulvestrant at the 250 mg dose indicated that ER α is still present at approximately 50% of the original baseline (Robertson J et al, Cancer Res 2001). It is unclear whether the lack of turnover of ER α represents poor drug exposure or lack of potency of fulvestrant on the ER receptor.

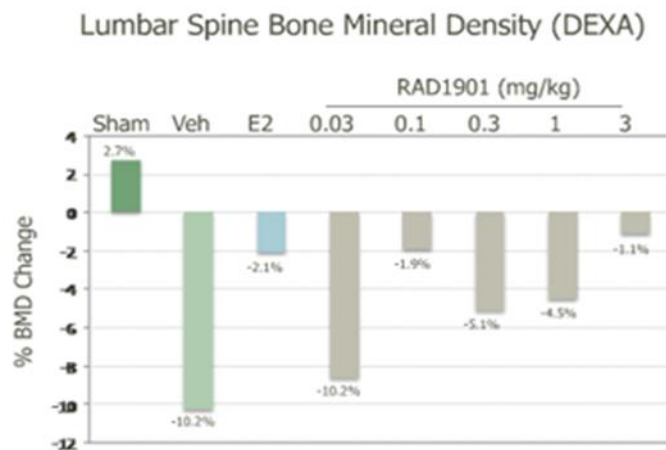
Therefore, development of second generation orally bioavailable SERDs needs to not only have high binding affinity to displace estradiol from the estrogen receptor, but it is also necessary to induce a conformational change of the receptor, rendering its function ineffective.

\$1.7B SERAGON ACQUISITION INTERESTING; MAY BE ADVANTAGEOUS FOR RAD1901

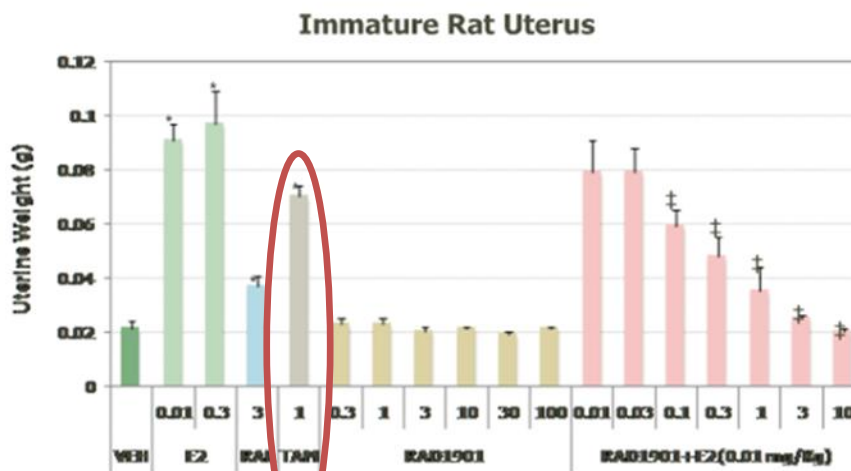
The recent acquisition of Seragon's SERD by Roche suggests interest in the HR+ MBC space, a positive for RAD1901. Similar to RAD1901, ARN-810 (developed by Seragon Pharmaceuticals) is also a SERD that showed promising Phase I data in advanced/metastatic ER positive BC. The company was later acquired by Roche earlier this year for \$725M in cash up front, plus up to an additional \$1B upon reaching certain milestones, reflecting the high interest in agents for MBC after hormone resistance.

In the Phase I data, ARN-810 was studied in post-menopausal women with advanced/metastatic ER positive breast cancer after progressing on initial hormone therapy. This was a safety, PD, and PK dose escalation study of ARN-810 administered orally. It is important to note that patients with untreated or symptomatic brain metastases were excluded. Pre- and post-treatment functional imaging with 18F-fluoroestradiol (FES)-PET was used to assess tumor ER binding and paired tumor biopsies to assess for ER target modulation by IHC and gene expression. Currently, two patients have been scanned with PET imaging. Patient number 1 had diffusely 18F-FES positive disease on the first scan, which converted to negative on scan 2 with therapy and new lesions developed. Patient number 2 had a single 18F-FES positive lesion on scan 1 that converted to negative on scan 2, but developed new hepatic lesions on the second scan, suggesting progression on study medication (Ayres K. *32nd Annual Vanderbilt University Research Forum* 2014). Because this data is preliminary and includes only two patients, we cannot make conclusions on the long term efficacy of the drug. Additionally, although this Phase I trial excluded patients with brain metastases, we do not have information yet if ARN-810 actually crosses the blood brain barrier until further data is presented YE14 at the San Antonio Breast Cancer Symposium.

When looking at the safety profile, RAD1901 may have less risk for endometrial cancer (high risk with tamoxifen) and bone loss (high risk with both tamoxifen and anastrozole), possibly permitting RAD1901 to earlier treatment settings in HR+ MBC. Figure 2 shows the bone mineral density score of an ovariectomized rat model, where the lack of estrogen decreased the bone mineral density by ~10.2% in the vehicle arm (potentially reflective of tamoxifen/anastrozole's effect on the bone). Administration of RAD1901 had similar protective effects on BMD as estrogen (E2) due to its selective estrogen agonist property. Additionally, because RAD1901 is highly selective, it does not stimulate the proliferation of ovarian and uterine tissues. Figure 3 represents immature rat uterus and the effects of RAD1901 and tamoxifen on uterine stimulation. Unlike tamoxifen, where expression in the uterus is high (circled in red), RAD1901 has minimum uptake in this area, eliminating the uterine cancer risk with tamoxifen that limits the drug's use.

Figure 2: RAD1901 Bone protective activity in rat OVX model**RAD1901 Protects Against Bone Loss in the Rat OVX Model**

Source: Radius Health investor presentation

Figure 3: Stimulation of uterus by tamoxifen and RAD1901**No Stimulation of the Uterus, and Antagonism of Estradiol Stimulation**

Source: Radius Health investor presentation

RAD1901 PENETRATING ~\$1.4B MARKET IN MBC

We estimate a total market opportunity of ~\$1.4B in patients with hormone receptor positive (HR+) MBC and HR+ BC with brain metastases. Please note that this model is just an assessment of the total market potential for RAD1901. Since the drug is currently in Phase I, we did not assign market share of RAD1901 into this model, nor did we include this model in our valuation of the company. However, due to the unique mechanism of action of RAD1901 compared to competitors and interesting data recently presented at the EORTC Brain Metastases conference, we believe there is significant potential for the drug to penetrate a large, untapped market.

Figure 4: Hormone positive metastatic breast cancer market opportunity

Total Metastatic BC Patients (HR+/HER2±)	~65,000 patients
Front line chemotherapy (40%)	~26,000 patients
Front line endocrine therapy (60%)	~39,000 patients
First line endocrine therapy (74%)	~28,900 patients
Price - \$2,500/month	
Duration – 10 months	
Total annual revenue	~\$720M
Second line endocrine therapy (19%)	~7,400 patients
Price - \$2,500/month	
Duration – 6 months	
Total annual revenue	~\$110M
Third line endocrine therapy (7%)	~2,700 patients
Price - \$2,500/month	
Duration – 3 months	
Total annual revenue	~\$20M
Total market opportunity	~\$850M

Source: Canaccord Genuity

Additionally, we evaluated the opportunity of RAD1901 in the MBC endocrine therapy (ET) landscape. Based on SEER data, there were ~50,000 patients with hormone receptor positive (HR+), HER2- disease and ~15,000 patients with HR+/HER2+ disease in 2013. Detailed epidemiology studies performed by Swallow et al reported 60% of front line metastatic patients receive ET, totaling ~39,000 patients (Swall et al. CMRO; 2014). Studies show that 74% of patients are on first line ET (~28,900 patients, mainly tamoxifen), 19% are on second line ET (~7,400 patients, split between aromatase inhibitors and fulvestrant), and 7% are on third line ET (~2,700 patients). Additionally, as the patient fails one line of therapy, the duration of subsequent therapies decreases from 10 months in first line to 3 months in third line use. Assuming a \$2,500 price target per month (fulvestrant is ~\$2,000/month), we estimate a market opportunity of ~\$850M for all endocrine use in MBC.

Figure 5: Hormone positive MBC with brain metastases market opportunity

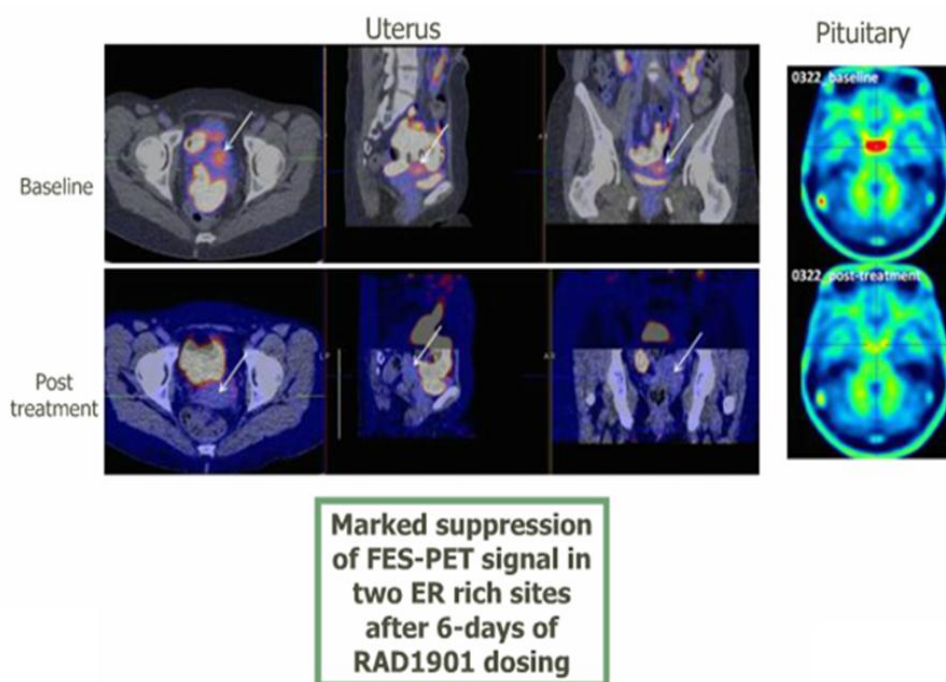
Total HR+ Metastatic BC with Brain Mets	~12,000 patients
Price - \$4,500/month	
Duration – 10 months	
Total market opportunity	~\$540M

Source: Canaccord Genuity

RECENT PHASE I UPDATE AT EORTC CONFERENCE PROMISING

New data from the Phase I MTD trial for RAD1901 was presented at the 4th Annual Brain Metastases Research and Emerging Therapies Conference on Sept. 19, 2014. Similar to ARN-810, this study also included a pharmacodynamics endpoint by using 18F-fluoroestradiol (FES)-PET to illuminate the estrogen receptor. Figure 6 shows the 18F-fluoroestradiol (FES)-PET uptake in the uterus and pituitary at baseline. When RAD-1901 was added, the ER signal in two ER rich sites was suppressed to background level at both low and intermediate doses. Interestingly, it only took six days for RAD1901 to suppress the estrogen receptor. Up to this point, 40 patients have been assessed with company guidance stating suppression of ER-signals at intermediate and lower doses. The trial has not maximized the dose of RAD1901 yet, and the company believes further dose escalation can result in increased efficacy. We expect a topline data readout at the end of this year at the San Antonio Breast Cancer Symposium. These results reflect positive proof-of-concept to move the trial into Phase 1B by YE14. Also, because of its ability to cross the blood brain barrier, RAD1901 is on track for Q4 protocol approval for two Phase 1b EORTC collaborative breast cancer trials with brain metastases, as well as on track for Q4 initiation of a EU trial in metastatic breast cancer.

Figure 6: 18F-fluoroestradiol (FES)-PET suppression by RAD1901



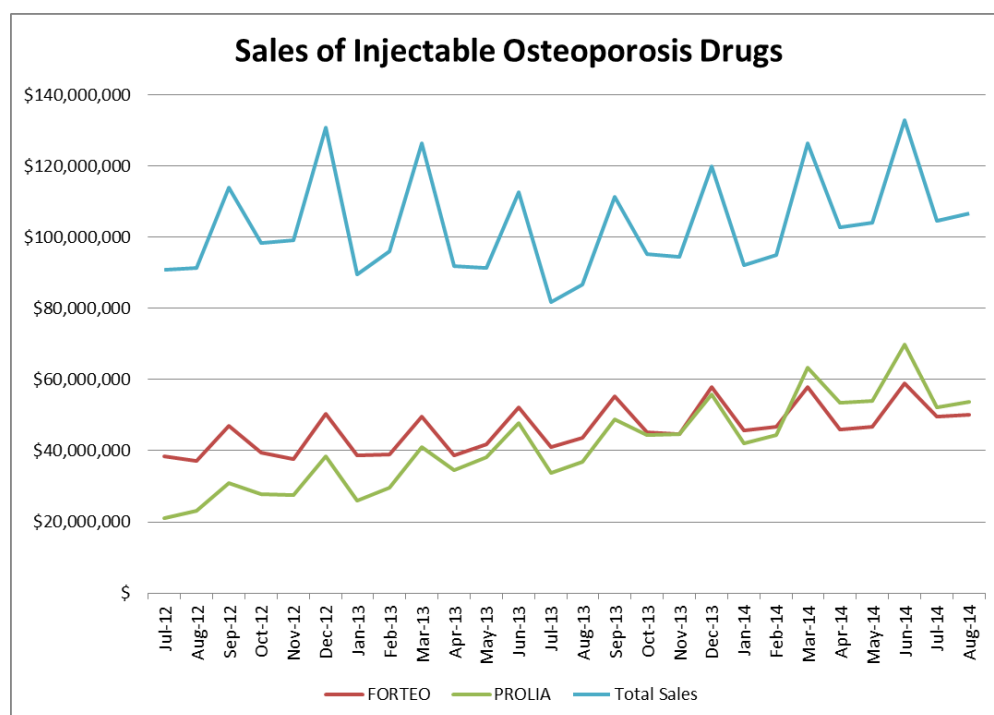
Source: Radius Health investor presentation

RAISING PRICE TARGET TO \$30 FROM \$26

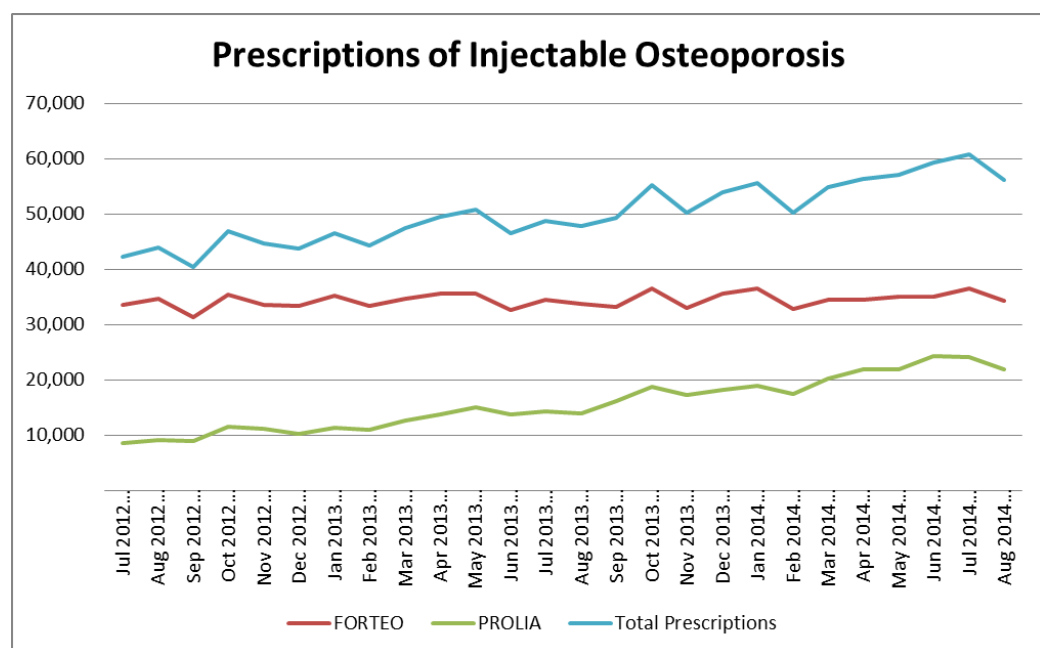
We are raising our price target to \$30 from \$26 given the increased demand for second line injectable osteoporosis drugs, specifically Forteo and Prolia, reflecting favorably for abaloparatide. For our analysis, we excluded IV Reclast and Boniva since they are in the bisphosphonate class. Figure 7 shows the sales of the two main injectable osteoporosis drugs currently on the market, with Prolia and Forteo increasing by an average of 3.80% and 1.08% per month, respectively. Figure 8 shows the increase in monthly prescriptions of Prolia and Forteo by an average of 2.6% and 0.09% per month, respectively. Total sales have increased by 2.26% and total prescriptions have increased by 1.15%, representing an expansion of the IV osteoporosis drug class. We have high confidence in positive Phase 3 data for abaloparatide to be presented YE14 that will show better efficacy data compared to Forteo. We view the Phase 3 trial as substantially de-risked based on prior head-to-head Phase 2 data versus Forteo showing superior BMD with less safety risk.

We are increasing our peak market share for abaloparatide to ~2.3% vs. ~1.5% previously, taking our US peak sales estimate to ~\$820M by 2022 vs. our prior estimate of ~\$650M. We believe that abaloparatide may expand the market for non-bisphosphonate injectable drugs due to potentially better efficacy and safety versus Forteo.

Figure 7: Sales of injectable osteoporosis drugs



Source: IMS database

Figure 8: Number of prescriptions of injectable osteoporosis drugs

Source: IMS database

VALUATION

Figure 9: Radius valuation

Product	Peak Sales (\$MM)	Year	NPV at launch	Probability Adjustment	Current Value (\$MM)	Scenario probability	Value / Share
abaloparatide							
US	\$822	2022	\$1,317	65%	\$666	100%	\$23
Ex-US - co-promote	\$346	2021	\$410	65%	\$181	50%	\$3
Ex-US - royalty	\$346	2021	\$196	65%	\$127	50%	\$2
Total abaloparatide					\$847		\$28
Total Product Value					847		\$28
Cash					60		\$2
Total Equity Value					907		\$30
Shares Outstanding (MM)					29		

Risk-Free Rate	3.0%
Beta	1.8
Risk Premium	5%
Discount Rate	12%

Source: Canaccord Genuity

Figure 10: Income statement

Radius Health, Inc.

(000's) [FY - DEC]

	2013A	1Q14A	2Q14A	3Q14E	4Q14E	2014E	2015E	2016E	2017E	2018E
Revenues										
abaloparatide - US								82,120	239,867	357,419
abaloparatide - Ex-US								-	90,548	204,751
Total								82,120	330,415	562,170
Income Statement	2013A	1Q14A	2Q14A	3Q14E	4Q14E	2014E	2015E	2016E	2017E	2018E
Total Revenue	-	-	-	-	-	-	-	82,120	264,315	457,747
COGS	-	-	-	-	-	-	-	16,424	52,863	91,549
Gross Profit	-	-	-	-	-	-	-	65,696	211,452	366,198
Operating Expenses										
Research and development	60,536	9,717	10,618	14,142	18,096	52,573	78,094	63,671	60,593	70,860
abaloparatide-SC	45,977	8,107	9,728	11,674	14,009	43,518	31,170	21,819	15,273	15,273
abaloparatide-TD	11,459	185	278	416	624	1,503	24,975	17,483	12,238	8,566
RAD1901	-	-	-	-	1,000	1,000	12,100	14,520	23,232	37,171
RAD140	-	-	-	-	-	-	-	-	-	-
other	3,100	1,425	1,710	2,052	2,462	7,649	9,850	9,850	9,850	9,850
General and administrative	6,829	2,139	3,070	2,500	2,700	10,409	13,200	57,484	85,902	102,993
Total Operating Expense	67,365	11,856	13,688	16,642	20,796	62,982	91,294	121,155	146,495	173,854
EBITDA										
Operating income	(67,365)	(11,856)	(13,688)	(16,642)	(20,796)	(62,982)	(91,294)	(55,459)	64,957	192,344
Other income (expense), net	9,085	(2,233)	1,727	1,727	1,727	2,948	9,350	2,948	9,350	2,948
Loss on retirement of note payable			(203)							
Interest (expense) income, net	(2,410)	(399)	(445)	(445)	(445)	(1,734)	(4,358)	(1,734)	(4,358)	(1,734)
Accretion of preferred stock		(4,969)	(4,031)							
Pre-tax income (GAAP)	(60,690)	(19,457)	(16,640)	(15,360)	(19,514)	(70,971)	(86,302)	(54,245)	69,949	193,558
Pre-tax income (non-GAAP)										
Taxes (GAAP)	-	-	-	-	-	-	-	-	25,881	71,617
Tax rate (GAAP)	37%	37%	37%	37%	37%	37%	37%	37%	37%	37%
Net Income (GAAP)	(60,690)	(19,457)	(16,640)	(15,360)	(19,514)	(70,971)	(86,302)	(54,245)	44,068	121,942
GAAP EPS (diluted)	(\$3.97)	(\$50.45)	(\$2.22)	(\$0.88)	(\$0.84)	(\$54.39)	(\$2.78)	(\$1.53)	\$1.18	\$3.11
Basic shares outstanding	15,278	386	7,500	17,400	23,200	12,121	31,539	35,562	37,340	39,207
Diluted shares outstanding	15,278	386	7,500	17,400	23,200	12,121	31,539	35,562	37,340	39,207

Source: Company reports and Canaccord Genuity estimates

Investment risks

Risks to our outlook and price target include the following: the Phase 3 study for abaloparatide in osteoporosis may be negative, or fail to meet investor expectations, resulting in downside to shares and our price target. Also, Phase 3 data may be positive in terms of efficacy, but show an unexpected safety signal, also resulting in downside to our price target. Antibody formation was been seen in Phase 2 studies, with one patient showing potential evidence of neutralizing antibodies.

Even assuming positive Phase 3 data for subcutaneous abaloparatide in osteoporosis, FDA approval may be delayed or may not occur at all, also resulting in downside to shares and our price target. FDA may also grant approval, but require large, lengthy and expensive post-approval studies, which could also result in downside to shares and our price target.

Clinical data from other osteoporosis products including anti-sclerostin antibodies from Amgen, Merck, Eli Lilly and Novartis could be viewed as superior to abaloparatide, pressuring shares. Competition from existing and new osteoporosis products could also result in lower revenues than expected, leading to downside to our estimates and the share price.

Although unlikely, a paragraph 4 challenge could be filed against Lilly's Forteo, a molecule closely related to abaloparatide, which investors may interpret as increasing risk for abaloparatide, and pressuring Radius shares. Forteo was approved as an NDA, where the ANDA pathway is well established. Even though Forteo is essentially a biologic, since it is a peptide, it is feasible although unlikely that a generic challenger could emerge. FDA has approved a generic version of Lovenox, a biologic approved via the NDA pathway, although the process took many years. If a generic version of Forteo were to reach the market, usage of abaloparatide could decline, resulting in downside to our estimates and price target. Also, if FDA were to approve a generic version of Copaxone, a peptide used to treat multiple sclerosis, investors may see increased risk of a generic challenge and approval for abaloparatide, as both products are classified as NDA filings for biologic peptides.

A transdermal microneedle formulation for abaloparatide may not be feasible, which investors may view as negative for life cycle management and commercial competitive positioning for Radius, pressuring shares. Even if a microneedle formulation can be developed to show equal efficacy to the subcutaneous formulation, FDA may require a full clinical study versus a bridging study, which would require additional funding and time to approval.

APPENDIX: IMPORTANT DISCLOSURES

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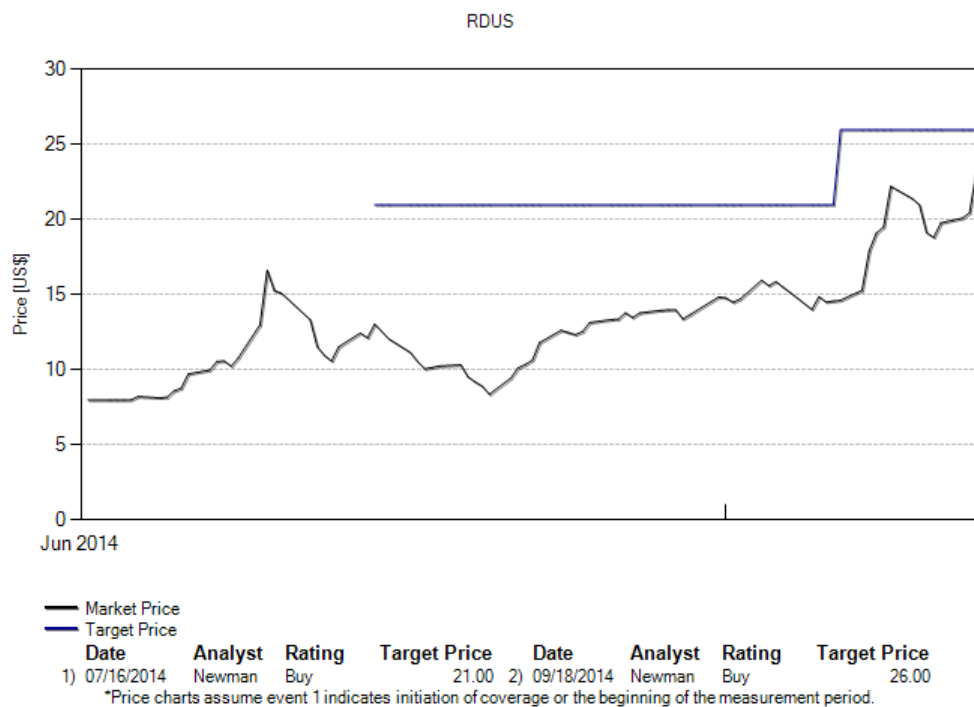
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Site Visit:

An analyst has visited Radius Health's material operations in Cambridge, Massachusetts. No payment or reimbursement was received from the issuer for the related travel costs.

Price Chart:***Distribution of Ratings:**

Global Stock Ratings
(as of 3 July 2014)

Rating	Coverage Universe		IB Clients %
	#	%	
Buy	602	61.2%	38.2%
Speculative Buy	49	5.0%	55.1%
Hold	290	29.5%	13.1%

Sell	41	4.2%	7.3%
	984	100.0%	

*Total includes stocks that are Under Review

**Canaccord Genuity
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BUY: The stock is expected to generate risk-adjusted returns of over 10% during the next 12 months.

HOLD: The stock is expected to generate risk-adjusted returns of 0-10% during the next 12 months.

SELL: The stock is expected to generate negative risk-adjusted returns during the next 12 months.

NOT RATED: Canaccord Genuity does not provide research coverage of the relevant issuer.

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Risk Qualifier:

SPECULATIVE: Stocks bear significantly higher risk that typically cannot be valued by normal fundamental criteria. Investments in the stock may result in material loss.

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Company	Disclosure
Radius Health	1A, 2, 3, 5, 7
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- | | |
|----|---|
| 13 | As of the month end immediately preceding the date of publication of this research, or the prior month end if publication is within 10 days following a month end, the relevant issuer owned 1% or more of any class of the total issued share capital in Canaccord Genuity or any of its affiliated companies. |
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