

# Alder Biopharmaceuticals (ALDR)

## SMALL & MID CAP RESEARCH



Rating	<b>OUTPERFORM*</b> [V]
Price (30 May 14, US\$)	10.74
Target price (US\$)	20.00 <sup>1</sup>
52-week price range	10.74 - 9.91
Market cap. (US\$ m)	321.16
Enterprise value (US\$ m)	262.45

\*Stock ratings are relative to the coverage universe in each analyst's or each team's respective sector.  
<sup>1</sup>Target price is for 12 months.

[V] = Stock considered volatile (see Disclosure Appendix).

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## Two Derisked Drugs and an Antibody Platform

We are initiating coverage with an Outperform rating and a \$20 target price. Our positive thesis is based on two derisked Phase II assets and an antibody platform that we expect will generate other highly potent drug candidates. We believe the primary value driver is its proprietary migraine drug ALD403, while its partnership with Bristol-Myers Squibb for clazakizumab provides non-dilutive milestone funding, clinical news flow with no clinical expenses, and potential future royalties.

- **Impressive Efficacy in Migraine:** A single infusion of ALD403 significantly reduced the number of migraines for an extended three-month period. Most impressively, 16% of patients were migraine free for three months versus 0% for placebo, and 32% had a 75% reduction in migraines in each of the three months versus 9% for placebo.
- **Lucrative Bristol Deal:** Clazakizumab is in Phase IIb testing for RA after demonstrating superiority to Humira in an earlier Phase II. We believe this program is high priority for Bristol and expect that ALDR could collect nearly all of the \$394M in pre-commercial milestones in RA over the next several years and midteen to 20% royalties on future sales. There are a total of \$745.5M in development and \$500M in sales milestones remaining.
- **Catalysts:** In the next 12 months, we expect (1) clazakizumab Phase II data in psoriatic arthritis, (2) the initiation of Phase III testing for clazakizumab in RA, and (3) the initiation of additional Phase II trials for ALD403.
- **Valuation:** Our \$20 target price includes \$15 for ALD-403, \$4 for Clazakizumab and \$1.50 for NOLs. We ascribe a 55% probability of success to ALD403 and first sales in 2019.

### Financial and valuation metrics

Year	12/13A	12/14E	12/15E	12/16E
EPS (CS adj.) (US\$)	-0.94	-1.10	-0.60	-1.85
Prev. EPS (US\$)	—	—	—	—
P/E (x)	-11.4	-9.8	-17.8	-5.8
P/E rel. (%)	-65.6	-61.3	-123.5	-44.8
Revenue (US\$ m)	18.8	18.7	59.3	25.3
EBITDA (US\$ m)	-19.8	-29.3	-19.2	-71.7
OCFPS (US\$)	-1.65	-1.68	-0.12	-2.36
P/OCF (x)	—	-6.4	-86.2	-4.5
EV/EBITDA (current)	-15.0	-10.2	-15.5	-4.2
Net debt (US\$ m)	-23	-59	-184	-90
ROIC (%)	37.60	82.64	41.19	303.60
Number of shares (m)	29.90	IC (current, US\$ m)		-55.22
BV/share (Next Qtr., US\$)	-1.6	EV/IC (x)		-6.1
Net debt (Next Qtr., US\$ m)	-15.0	Dividend (current, US\$)		—
Net debt/tot eq (Next Qtr., %)	42.4	Dividend yield (%)		—

Source: Company data, Credit Suisse estimates

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# Portfolio Manager Summary

## Platform—Antibody Production in Yeast

ALDR was founded in 2004 on its technology to optimize antibody production, using a novel yeast production system. This technology overcomes many of the limitations of traditional antibody manufacturing: (1) low cost of production in yeast, (2) rapid scale up and high yields with the manufacturing process, (3) generation of a clinical candidate in a short period of time, and (4) ability to apply this technology to a wide range of therapeutic areas.

In practice, the technology has been validated by the generation of two clinically proven drug candidates, with demonstrated high potency for their target, long half-life, low immunogenicity, and high manufacturing yields. These successes provide validation of both the platform and the process/expertise of the team.

## Derisked Pipeline

ALDR has generated two candidates from its platform with substantial positive clinical data, and we anticipate ALDR will bring at least one new clinical candidate forward in 2014 to start Phase I in 2015.

- **Proprietary Drug for Migraine:** The most valuable program, in our opinion, is the anti-CGRP antibody for migraine (ALD403). The first proof-of-concept data were recently presented at the 2014 AAN meeting (May 2014), demonstrating a statistically significant and clinically important benefit in the prevention of migraines. This program is 100% owned by ALDR.
- **Partnered Drug:** Bristol Myers-Squibb is developing clazakizumab, an anti-IL6 antibody for RA and psoriatic arthritis. Head-to-head Phase II data showed superiority of a clazakizumab-based regimen compared with a Humira regimen in RA, and Phase III trials are expected to start in 2015. BMY covers all development costs, and ALDR is eligible to receive significant milestones (\$746M pre-commercial and \$500M in sales milestones) and double-digit royalties up to 20%. Importantly, there are \$394M in pre-commercial milestones just for the RA program, which we believe have a high probability of being earned.
- **Pipeline:** ALDR has four preclinical stage programs, with two programs in the pain setting and two are in an orphan disease setting. ALDR expects to select the next candidate in H2:14 and plans to file an IND in H1:15, with the clinical studies expected to start in mid-2015. We expect investors will begin to value the pipeline as new candidates are disclosed and clinical timelines are announced.
- **Technology:** ALDR's novel antibody production system has several advantages including low cost of goods, which may become important in competitive markets (RA) or potentially price sensitive markets (migraine).

## The Antibody Investment Thesis:

We recommend investors have broad exposure to the antibody subsector of the biotechnology space to take advantage of three continuing trends: (1) antibodies have a higher clinical success rate, (2) pharmaceutical companies and some large biotechs still have a need for more biologics, and (3) next-generation technologies offer significant long-term growth.

**Exhibit 1: ALDR Pipeline**

Drug	Target	Indication	Stage	Partner
Clazakizumab	IL-6	Rheumatoid Arthritis	Phase IIb	Bristol-Myers Squibb
		Psoriatic Arthritis	Phase II	Bristol-Myers Squibb
ALD403	CGRP	Migraine	Phase II	Proprietary
4 preclinical programs	TBA	TBA	Preclinical	Proprietary

Source: Company data, Credit Suisse research.

**Exhibit 2: ALDR News Flow**

Product	Catalyst	Expected Date
Clazakizumab	Updated Phase IIb RA data at EULAR	June 2014
ALD403	Start Phase IIb dose ranging study	H2:14
Clazakizumab	Phase IIb dose exploration data in RA	H2:14
New target	Select new clinical stage candidate	H2:14
Clazakizumab	Phase II data in psoriatic arthritis	YE-2014
Clazakizumab	Phase III start	2015
ALD403	Phase IIb data	H2:15
New target	First clinical study start (one or more)	H2:15
ALD403	End of Phase II meeting with FDA	YE:15
ALD403	Start Phase III in migraine	2016
ALD403	BLA submission	Mid-2018
Clazakizumab	BLA submission	2018
ALD403	Potential approval	H1:2019
ALD403	Potential launch	Mid-2019

Source: Company data, Credit Suisse estimates.

## Investment Positives

- **Impressive Data in Migraine:** ALDR is developing ALD403, its wholly owned anti-CGRP antibody, as a prophylactic to prevent migraines. We believe that this new class of drugs will gain significant physician and investor interest over the next few years, and recent data at AAN in May 2014 provided a first look. ALDR reported that 16% of patients went from around eight migraines days per month to zero migraines over three months with a single dose. A 75% reduction in migraines (in all three months) was achieved in 32% of ALD403 patients versus 9% for placebo.
- **Multibillion Dollar Market Potential in Migraine:** We believe migraine prevention is a potential multibillion dollar drug class in the U.S., with significant ex-U.S. partnering opportunities. In the U.S., there are approximately 7 million patients diagnosed with high frequency episodic migraines (5-14 migraine days per month) and another 3 million patients with chronic migraines (15 or more migraine days per month). We take a smaller cut of this 10M patient pie including only those treated by specialists and only the upper end of high frequency episodic (9-14 migraine days per month). Assume a \$10,400/year gross price, 15% gross to net, 75% compliance, and 20% penetration for the entire drug class, we arrive at a market estimate of \$5.3 billion in 2022.
- **Strong Data for Clazakizumab in RA:** In a head-to-head Phase II trial, single-agent clazakizumab was as effective as standard of care Humira plus methotrexate, and the combination of clazakizumab plus methotrexate was superior. These results are being confirmed in a larger Phase IIb trial and a separate Phase II program is ongoing in psoriatic arthritis.
- **Large Market for Biologics in RA:** The market for biologics in RA and related autoimmune diseases is approximately \$18 billion in the U.S. While the space is crowded with competitors, IL-6 inhibitors are increasing market share, and we suspect the class will grow to greater than \$2 billion. Bristol would compete against Roche's Actemra and potentially Sanofi/Regeneron's sarilumab. High potency and low cost of goods could provide some competitive advantages.
- **Large Partnership with Bristol-Myers Squibb:** BMJ is responsible for all clinical development expenses, and ALDR is eligible for double-digit royalties (up to 20%) and significant pre-commercial and sales milestones. Currently, there are \$745.5M in development milestones remaining, including \$348M in RA, and \$500M in sales milestones. In our view, the pre-commercial RA milestones have a high probability of

being earned, as the program has already shown good efficacy and the drug class is largely derisked.

- **Platform Technology Is Clinically Validated:** ALDR has validated its yeast production system with the development of two active, clinical stage candidates. ALDR's yeast production generates high potency, long half-life antibodies with very low cost of goods. The clinical trials for ALD403 and clazakizumab have shown that the antibodies generated by its platform and produced in yeast are safe and well tolerated. This is important because both markets, migraine and RA, are markets that require chronic therapy.

## Investment Risks

- **CGRP Competition Is Heating Up:** There are several anti-CGRP antibodies in development for migraine prevention, including drugs from AMGN, LLY, and Labrys (private). To date, we have only seen data from ALDR and LLY, although AMGN and Labrys have advanced into larger Phase II trials. It is possible that one or more of these programs could advance faster or generate better clinic data. At a minimum, we expect ALDR will compete commercially with one or more of these competitors. In our model, we conservatively give ALDR 20% of the anti-CGRP market.
- **Unexpected negative result for ALD403.** Current data is still early. While the clinical data for ALD403 have been impressive, the trial only tested a single infusion. The dose and schedule have not been determined and long-term safety has not been established. It is possible that safety issues could emerge with repeat dosing or that establishing the optimal dose and schedule could take longer than anticipated.
- **Migraine Prophylaxis Market Is Underdeveloped:** Migraine prophylaxis with currently approved small molecules is limited by inadequate efficacy and tolerability issues. Currently, the only biologic approved for migraine prophylaxis is Botox, which requires up to 31 injections in the head and neck. ALDR and other anti-CGRP competitors will need to grow the market for injectable drugs for migraine prophylaxis.
- **RA Space Is Crowded:** There are multiple approved biologic drug classes for treating RA including anti-TNF, anti-CD20, anti-IL6, and others. New oral agents are also affecting the use of biologics in RA. Clazakizumab will need to compete with other anti-IL6 therapies including Actemra (currently marketed) and Sarilumab (Phase III)
- **Financing Risk:** We anticipate that ALDR will need to raise additional capital to fund its plans to advance ALD403 to the market. Capital needs may be reduced if milestones are earned from BMJ and/or commercial rights are licensed in territories outside the U.S. We project another capital raise by YE:15.

## Valuation: \$20 Target Price

Our \$20 valuation is justified by a fully-taxed, probability weighted, product-level DCF for each of the two clinical stage programs plus the value of future NOLs. We assume an ex-U.S. partner for ALD403 and significant dilution from future equity raises prior to profitability. For our DCF analysis, we use a 12% discount rate and a 35% tax rate.

Our valuation is purposefully conservative in the following ways: (1) we exclude value for the preclinical pipeline and antibody platform, (2) we assume relatively low probabilities of success for products that have good Phase II data, (3) we model a relatively low penetration for clazakizumab, and (4) we assume substantial dilution in our per-share calculations.

- **ALD403 (\$15/share):** We assign a 55% probability of success and probability weight future sales and launch/selling expenses. We model approximately \$700/month at

launch, growing at 2% per year. We assume a 2019 launch and peak U.S. penetration in 2022, which includes 20% penetration of the anti-CGRP class into the high frequency episodic and chronic migraine population, and a 15-20% share of that market for ALD403. We estimate unadjusted global sales in 2022 at approximately \$1.06 billion (\$913M U.S.; \$145M ex-U.S.).

- **Clazakizumab (\$4-6/share):** We assign a 40% probability of success and probability adjust preapproval milestones to a lesser extent. Approximately 70% of the value of the clazakizumab program is in the milestones based on our conservative sales assumptions. We assume launch in 2019 and peak U.S. penetration in 2024, with global sales that year of \$537M. Because ALDR has a passive interest in clazakizumab, with no further expenses required, one could argue that the value should be divided by current shares rather than future shares (which account for future cash needs to fund ALD403 and the pipeline). Using current shares as the denominator, the value of clazakizumab increases to \$6/share.
- **NOLs (\$2/share):** Because we fully tax the DCF for each product and assume future equity raises in our share denominator, we include the NPV of the tax benefit of the forecast NOLs accumulated through to profitability.
- **Pipeline (Not Valued):** We do not assign value in our target price for ALDR's antibody platform and unnamed preclinical candidates. We expect our target price could be positively affected as new candidates are disclosed and move into the clinic. We also view the discovery engine as an essential part of the ALDR story.

#### Exhibit 3: Sum of the Parts Valuation

Program	NPV (\$M)	Sales* (\$M)	POS	Per share (current)	per share (future)
ALD403	\$743	\$1,057	55%	\$23	\$15
Clazakizumab	\$194	\$537	40%	\$6	\$4
NOLs (future)	\$76			\$2	\$2
<b>Total</b>	<b>\$1,013</b>			<b>\$31</b>	<b>\$20</b>

\* ALD403 sales in 2022 and clazakizumab sales in 2024

Source: Company data, Credit Suisse estimates.

#### Exhibit 4: ALDR Income Statement

	2012A	2013A	2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E
<b>Revenues</b>											
US sales of ALD403								29.7	154.6	361.8	501.9
Ex-US royalties on ALD403									0.7	5.8	21.7
Royalties on Clazakizumab								2.4	5.3	11.2	18.0
Collaboration and license agreement	20.1	18.8	18.7	59.3	25.3	7.5	103.1	197.6	62.3		35.0
<b>Total Revenues</b>	<b>20.1</b>	<b>18.8</b>	<b>18.7</b>	<b>59.3</b>	<b>25.3</b>	<b>7.5</b>	<b>103.1</b>	<b>229.8</b>	<b>222.8</b>	<b>378.8</b>	<b>576.6</b>
<b>Expenses</b>											
Cost of goods								3.0	15.5	36.2	50.2
Research and development	30.7	31.9	36.5	58.5	74.0	90.0	92.0	87.0	77.0	75.0	72.0
Sales, general, administrative	7.2	7.7	12.5	21.0	24.0	24.0	26.0	35.0	40.0	45.0	40.0
<b>Total Operating Expenses</b>	<b>37.9</b>	<b>39.6</b>	<b>49.0</b>	<b>79.5</b>	<b>98.0</b>	<b>114.0</b>	<b>118.0</b>	<b>122.0</b>	<b>117.0</b>	<b>120.0</b>	<b>112.0</b>
Operating income (loss)	(17.8)	(20.8)	(30.3)	(20.2)	(72.7)	(106.5)	(14.9)	107.8	105.8	258.8	464.6
Total Other Income (Expense)	0.0	0.1	0.0	0.0	0.0	0.0	0.2	0.2	0.2	0.2	0.2
Pre Tax Income	(17.8)	(20.6)	(30.2)	(20.2)	(72.7)	(106.5)	(14.7)	108.0	106.0	259.0	464.8
Income tax										90.6	162.7
<b>Net Income</b>	<b>(17.8)</b>	<b>(20.6)</b>	<b>(30.2)</b>	<b>(20.2)</b>	<b>(72.7)</b>	<b>(106.5)</b>	<b>(14.7)</b>	<b>108.0</b>	<b>106.0</b>	<b>168.3</b>	<b>302.1</b>
<b>EPS - diluted (proforma)</b>	<b>(\$3.55)</b>	<b>(\$3.84)</b>	<b>(\$1.10)</b>	<b>(\$0.60)</b>	<b>(\$1.85)</b>	<b>(\$2.26)</b>	<b>(\$0.31)</b>	<b>\$2.09</b>	<b>\$2.03</b>	<b>\$3.18</b>	<b>\$5.64</b>
Shares outstanding - basic (proforma)	5.01	21.89	27.61	33.34	39.31	47.16	47.99	48.47	48.95	49.44	49.94
Shares outstanding - diluted (proforma)	5.01	21.89	27.61	33.34	39.31	47.16	50.97	51.60	52.24	52.90	53.56

Source: Company data, Credit Suisse estimates.



## The Antibody Investment Thesis

ALDR fits nicely within our bullish antibody investment thesis. We recommend investors have broad exposure to the antibody subsector to take advantage of three continuing trends: (1) higher clinical success rates, (2) industry consolidation by pharma and big biotech needing more antibodies, and (3) next-generation technologies.

**Own the Group:** Investors have and we believe will continue to benefit from broadly owning the antibody sector. We favor companies with large pipelines, substantial funding from partners, and strong proprietary technologies. ALDR fits these criteria.

**Antibody Companies Have a Good Track Record for Investors:** There is upside potential, as standalone companies (ALXN, REGN, SGEN, etc.) and premium take outs (DNA, IMCL, FACT, MEDX, HGSI, etc.) have been the historical norm among antibody companies. Our top two pure plays are REGN and SGEN, but we continue to recommend that investors own a basket of these stocks including the emerging smaller-cap companies.

- **Higher Success Rates:** The success rate at each stage of development is higher with antibodies than with traditional pharmaceuticals. Higher specificity, lack of active metabolites, predictable drug properties, and the growing use of diagnostics have and will likely continue to make antibody drug development lower risk.
- **History of Acquisitions:** Pharma and large-cap biotech have a history of acquiring antibody companies. Companies with technology platforms and retained rights are likely the most attractive targets. ALDR's successful discovery engine and unique manufacturing platform along with retained rights to its migraine program make it an attractive target.
- **Growing Focus on Next-Generation Drugs:** Ultra-potent antibodies, including higher affinity antibodies or technologies to increase antibody efficacy, are proliferating. Increased affinity is leading to less frequent dosing in some cases (a competitive advantage for injectables), lower cost of goods, and new market opportunities. ALDR combines high potency with low cost of goods to potentially open new markets that might otherwise be more difficult to penetrate with expensive biologics.
- **Safety of Antibodies Is Ideal for Chronic Therapies:** Antibodies are known for lacking "off-target" toxicity, so if the target of the antibody is chosen appropriately, the risk of unwanted side effects is low.

**Exhibit 5: Attractive Public Comps for Antibody Platform**

Company	Ticker	Price 5/30/14	Market Cap. (MM)	Enterprise Value (MM)
Seattle Genetics	SGEN-US	\$33.37	4,252.2	3,754.0
Morphosys	MOR:GR	\$92.09	2,404.5	2,008.0
Celldex	CLDX-US	\$14.30	1,277.8	1,003.6
ImmunoGen	IMGN-US	\$11.82	992.9	850.2
Merrimack	MACK-US	\$8.10	837.6	827.4
Oncomed	OMED-US	\$23.63	698.4	414.5
Ablinx	ABLX-BT	\$12.15	593.3	500.1
MacroGenics	MGNX-US	\$20.44	564.6	370.1
Xoma	XOMA-US	\$4.22	451.1	370.4
Alder Biopharmaceuticals	ALDR-US	\$10.46	322.2	217.3
Five Prime	FPRX-US	\$13.90	298.0	169.1
Xencor	XNCR-US	\$8.56	268.5	190.5
<b>Average</b>			<b>1,080.1</b>	<b>889.6</b>
<b>Median</b>			<b>645.8</b>	<b>457.3</b>

Source: Company data, Credit Suisse research.

# Market Model for ALD403 in Migraine

We model first ALD403 sales in 2019 and peak share in 2022. Our model projects \$913M in U.S. sales at a peak penetration of approximately 20% (\$502M probability adjusted). We estimate that ex-U.S. sales in the same settings will reach ~\$900M with a three year lag (~\$500M probability adjusted).

- **Pricing:** We assume that at launch ALD403 is priced at \$10,000 per year gross (~\$700 per month, with 15% gross to net adjustment) and increases 2% per year thereafter.
- **U.S. Market Size:** In the U.S., where we assume ALDR will market the drug itself, we use a starting population of 5.3M migraine patients treated by specialists, with 2.1M at the upper end of high-frequency episodic migraines (9-14 days/month) and 1.6M patients with chronic migraines (15+ days/month). We assume that approximately 20% of these patients elect to use an anti-CGRP therapy and that peak penetration for ALD403 in this market reaches 20%. This implies ~135,000 patients on ALD403 in 2022, which we believe is reasonable and conservative, given we estimate there will be approximately 5.6M migraine patients receiving therapy.
- **Ex-U.S. Market:** We assume that ALDR signs an ex-U.S. partner with milestones and royalties. We model an ex-U.S. royalty of 15%.
- **Risk-Adjusted Market Model:** We assume a 55% probability of success. While the probability of success is relatively high for a Phase II asset with minimal clinical data, we believe that the program has lower risk owing to the target being well validated and with other therapies directed against the same pathway demonstrating efficacy in the migraine setting.

## Exhibit 6: ALD403 Market Model in the U.S.

	2019	2020	2021	2022	2023	2024	2025
Patients Treated for Migraines by a Specialist	5,296	5,402	5,510	5,620	5,733	5,848	5,964
Patients Treated for Episodic Migraines (9-14 migraines)	2,119	2,161	2,204	2,248	2,293	2,339	2,386
CGRP mAb Drug Class penetration	4%	8%	15%	20%	20%	20%	20%
ALD403 share	7.5%	15.0%	15.0%	15.0%	15.0%	15.0%	15.0%
Treated	6	26	50	67	69	70	72
Treatments/ year	6.00	7.50	9.00	9.00	9.00	9.00	9.00
Net price/dose	\$708	\$723	\$737	\$752	\$767	\$782	\$798
<b>Sales - US (M)</b>	<b>\$27.0</b>	<b>\$140.5</b>	<b>\$328.9</b>	<b>\$456.3</b>	<b>\$474.7</b>	<b>\$493.9</b>	<b>\$513.8</b>
Patients Treated for Chronic Migraines (≥15 migraines)	1,589	1,621	1,653	1,686	1,720	1,754	1,789
CGRP mAb Drug Class penetration	4%	8%	15%	20%	20%	20%	20%
ALD403 share	10.0%	20.0%	20.0%	20.0%	20.0%	20.0%	20.0%
Treated	6	26	50	67	69	70	72
Treatments/ year	6.00	7.50	9.00	9.00	9.00	9.00	9.00
Net price/dose	\$708	\$723	\$737	\$752	\$767	\$782	\$798
<b>Sales - US (M)</b>	<b>\$27.0</b>	<b>\$140.5</b>	<b>\$328.9</b>	<b>\$456.3</b>	<b>\$474.7</b>	<b>\$493.9</b>	<b>\$513.8</b>
<b>Total Sales - US (M)</b>	<b>\$54</b>	<b>\$281</b>	<b>\$658</b>	<b>\$913</b>	<b>\$949</b>	<b>\$988</b>	<b>\$1,028</b>
COGS	\$5	\$28	\$66	\$91	\$95	\$98.78	\$103
Probability adjusted Sales - US (M)	\$30	\$155	\$361.82	\$502	\$522	\$543	\$565
Probability adjusted COGS	\$2.97	\$15	\$36	\$50	\$52	\$54	\$57
Ex-US sales (000) unadjusted		\$8.1	\$70.3	\$263.1	\$547.5	\$759.5	\$889.0
Ex-US sales (000) Probability adjusted		\$4.5	\$38.6	\$144.7	\$301.1	\$417.7	\$489.0
<b>ROW Royalties</b>		<b>\$0.7</b>	<b>\$5.8</b>	<b>\$21.7</b>	<b>\$45.2</b>	<b>\$62.7</b>	<b>\$73.3</b>

Source: Company data, Credit Suisse estimates.

# Market Assumptions for Clazakizumab

We model first clazakizumab U.S. sales in 2019 and peak share in 2023, followed by growth via population growth and price increases. Our model projects \$526M in global peak sales at peak penetration in 2023 (\$210M probability adjusted). Sales grow from there based on price and population. Several of these assumptions have built-in conservative estimates.

- **Pricing:** We assume initial gross price in 2019 of \$18,600 (\$1,320 per month, with a 15% gross-to-net adjustment).
- **Royalties:** Our model assumes tiered royalties (high-double digits to 20%) and milestones from BMJ. We assume BMJ covers all of the program's costs through development and regulatory milestones.
- **Market Size:** We assume roughly 21,400 patients on treatment at peak penetration in 2023. This is only a small fraction of the total biologics market.
- **Risk-Adjusted Market Model:** We assume a 40% probability of success, which is applied to the NPV of the unadjusted royalty stream.
- **Milestones:** We assume that the probability of pre-commercial milestones is higher than the overall probability of success (85% for Phase III start). Since these are large and front loaded, the value of the program is largely tied to the milestones (~70% of the value in our model). (See Exhibit 8.) We show the milestone assumptions for RA for example and have a similar analysis for psoriatic arthritis. (See Exhibit 7.)

**Exhibit 7: Milestone Probability and NPV**

Rheumatoid arthritis			
Milestone	Prob.	Amt.	Adjusted
	100%	15	
Phase 3 start	85%	40	34
BLA filing	50%	60	30
MAA filing	50%	36	18
BLA approval	40%	105	42
MAA approval	40%	100	40
Japanese filing	45%	18	8.1
Japan approval	40%	35	14
Total		409	186.1
NPV			77.4

Source: Company data, Credit Suisse estimates.

**Exhibit 8: Value of Clazakizumab is Largely in the Milestones**

NPV analysis		
		% of total
Milestones	136.0	71%
RA	57%	
PsA	26%	
Sales	17%	
Royalty	56.5	29%
Total for claza	192.5	

Source: Company data, Credit Suisse estimates.



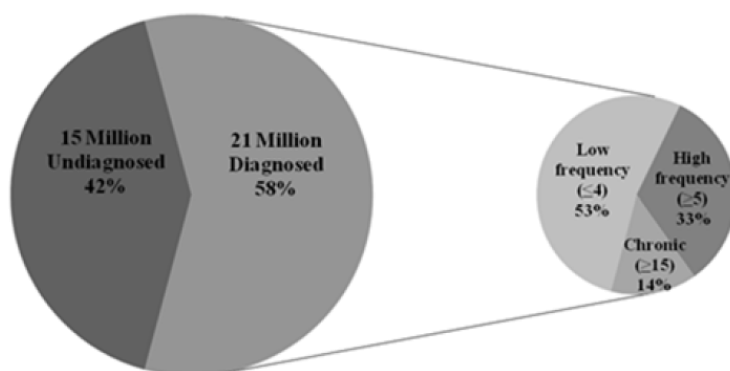
# ALD403 for Migraine Prevention

## Brief Migraine Overview

An estimated 36M people in the U.S. suffer from migraines, and approximately 21M have received a migraine diagnosis. (See Exhibit 9.) There are two major categories of migraine, episodic (<15 days per month) and chronic ( $\geq 15$  days per month). Episodic migraine patients are often categorized as low frequency (<5 migraine days per month) or high frequency (5 to 14 migraine days per month). Patients with episodic migraines can progress to become chronic migraine sufferers.

The likely target market for new biologics for prophylaxis includes patients with high-frequency episodic (5-14) and chronic ( $\geq 15$ ) migraine days. ALDR estimates there are approximately seven million high-frequency episodic migraine patients and about three million chronic migraine patients. ALDR estimates that 6.6M migraine patients receive treatment and the remaining do not.

**Exhibit 9: Breakdown of the Migraine Market by Migraine Days**



Source: ALDR S-1.

## Standard of Care

Migraine patients with fewer than five headaches a month are typically treated only with acute abortive medication. The goal of abortive medication is to stop or reduce the intensity of a migraine once it has begun. These treatments include triptans and NSAIDs, and the standard measure of efficacy is pain relief or pain free within two hours. Triptans are contraindicated for patients with cardiovascular disease and otherwise healthy patients can only take a modest total dosage of triptans each month.

Patients who have five or more migraine days per month may be candidates for prophylaxis to reduce the frequency of the migraines. Currently, the only approved medication for chronic migraines (15+ migraine days per month) prophylaxis is Botox. Topomax (topiramate) is approved for migraine prophylaxis but was only studied in patients with episodic migraines.

- Botox requires 31 shots in the head and neck once every three months. The prophylactic benefit provided by Botox is limited, as it has only been associated with a 47% increase in patients that reported a 50% improvement in migraine days or migraine frequency per month (within six months). Allergan reported 2013 sales of approximately \$1.07B for the Botox Therapeutic franchise, of which we estimate ~\$200M is for sales in migraine (AGN does not disclose sales by indication).
- Topomax is approved for both migraine and for epilepsy. The chronic use of Topomax for migraine prophylaxis is limited by its modest efficacy and side-effect profile

including paresthesia, nausea, anorexia, diarrhea, and memory problems. Adherence to current prophylaxis is low.

**Exhibit 10: Standard of Care by Patient Segmentation**

Segment of Migraine Market	Therapy Goal	Agents
Acute care	Abortive treatment (pain relief within 2 hours)	Triptans* and NSAIDs*
Preventive care (High frequency episodic: 5-14 days/month and Chronic: 15+ days/month)	Prophylactic treatment (reduction of # of headache days / month)	Botox and Topiramate*

\* Generic products available

Source: Company data, Credit Suisse research.

### Targeting CGRP: A Therapy Designed Specifically for Treating Migraines

CGRP or calcitonin gene related peptide is a 37 amino acid neuropeptide that is expressed in the sensory neurons, and it is believed to be involved in pain signaling and the initiation of migraines. CGRP has been shown to act on the peripheral and central nervous system. Serum CGRP levels increase upon migraine initiation and return to normal levels concurrently with migraine relief. Migraines can be triggered in patients susceptible to migraines with the administration of CGRP, suggesting that this is an important pathway in migraine pathology.

CGRP was previously an exciting target for migraine therapy, but it lost its shine after a Merck small molecule drug failed in the clinic due to liver toxicity. The liver toxicity is most likely associated with the specific chemistry of the small molecule drugs and not the target, as no liver toxicity issues have been seen to date for the anti-CGRP antibodies.

### ALD403—A New Antibody Targeting CGRP

ALD403 binds free serum CGRP and prevents it from interacting with its receptor. Prophylaxis with ALD403 is believed to protect against the initiation of migraines via CGRP, and recent clinical data support this mechanism of action. ALD403's primary mechanism of action is believed to be in preventing the interaction of CGRP with the peripheral nervous system, as it does not cross the blood brain barrier.

### ALD403 Clinical Data to Date

The current clinical trials of ALD403 test an IV formulation, although a subcutaneous injection is also being developed. Clinical data now support the safety and efficacy of a single infusion, the feasibility of subcutaneous dosing, and safety in combination with triptans. The high potency and long half-life of ALD403 may reduce the frequency of administration and serve as a differentiating characteristic for the antibody.

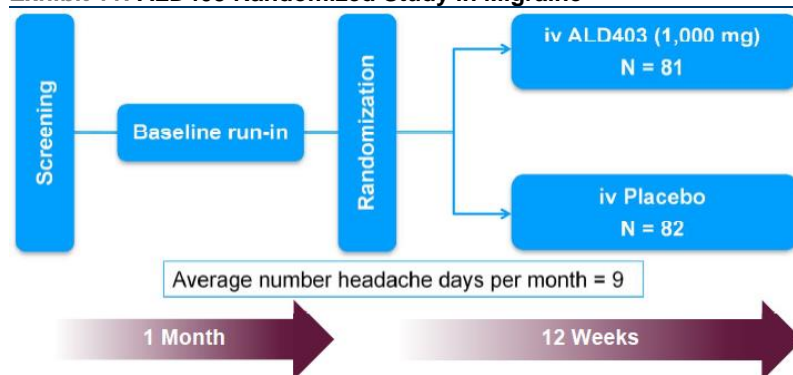
Alder recently completed a randomized, double blind, placebo-controlled Phase I proof-of-concept study with 163 patients with high frequency migraines (5-14 migraine days per month). A single 1000 mg dose of ALD403 was administered to the patients that had an average of eight migraine days per month (nine headache days per month). Patients were followed for six months after the single initial dose, and results for the first three months were recently presented at the AAN meeting in May 2014.

ALDR provided two types of efficacy measurements. The first is the standard reduction in migraine days over time and the second was a more impressive responder analysis, including the very stringent 100% response criteria. Both criteria were met with statistical

significance. The durability of the response rate over three months was impressive, given it was a single infusion of ALD403.

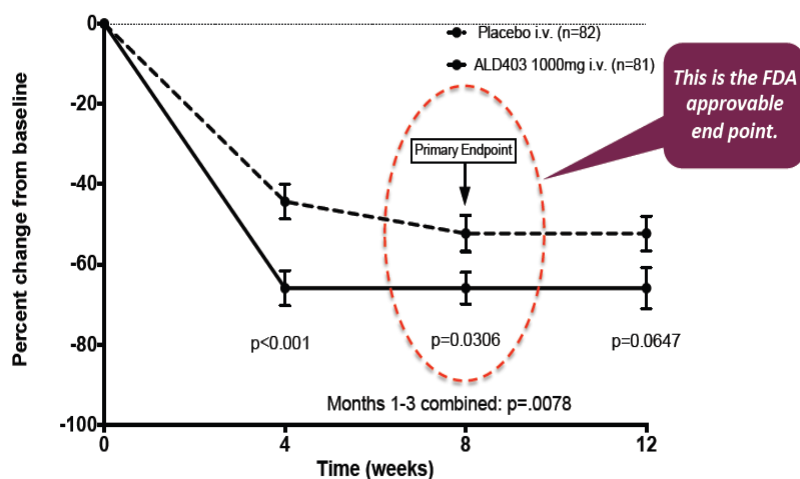
- **Migraine Days:** The mean reduction in migraine days was statistically significant at week 8 (the standard FDA measure of efficacy), with a p value of 0.031. (See Exhibit 12.) The onset of activity was rapid, with statistical significance at week 4. Although still better than placebo at week 12, the result was no longer statistically significant ( $p=0.0647$ ).
- **Responder Analysis:** ALDR defined a response as meeting the criteria for a specific level of reduction in migraine days (e.g., 50%, 75%, or 100%) in each of the three months following administration of ALD403 or placebo. By the most stringent 100% criteria, ALD403 eliminated migraine days in all three months in 16% of the patients versus 0% of placebo patients, which is an unprecedented result. (See Exhibit 16.) Additionally, 32% of the patients had a 75% reduction in migraine days (versus 9% for placebo), and 60% of the patients had a 50% reduction in migraine days (versus 33% for placebo).

**Exhibit 11: ALD403 Randomized Study in Migraine**

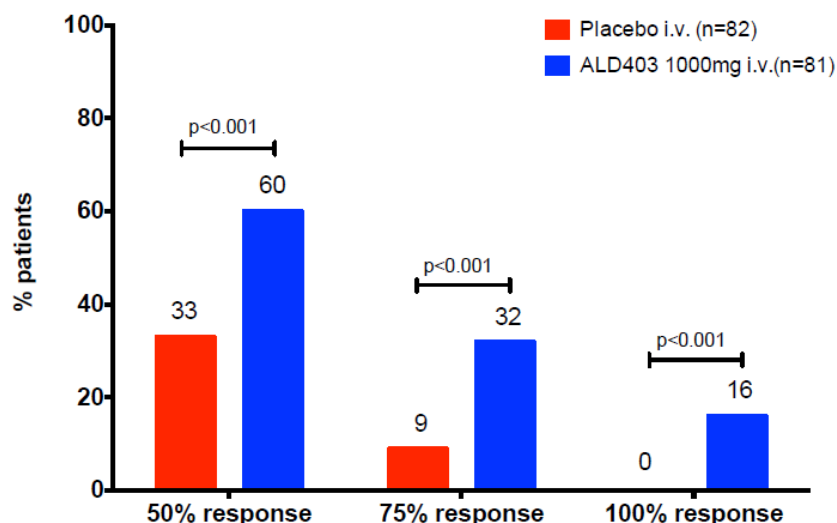


Source: Company data, Credit Suisse research.

**Exhibit 12: Reduction in Migraine Days with ALD403**



Source: Company data, Credit Suisse research.

**Exhibit 13: Responder Analysis for All Three Months—Impressive 100% Response**

Source: Company data, Credit Suisse research.

### Safety with Triptans

There is no evidence for any increase in toxicity in combination with commonly prescribed triptans.

In a separate Phase I study analyzing the safety of ALD403, a small subset of patients received 300 mg of ALD403 IV or placebo four hours before receiving 6 mg of sumatriptan subQ. These patients were then followed and examined with numerous cardiovascular tests. This portion of the study demonstrated that ALD403 is well tolerated with triptan co-administration, including no increase in systolic or diastolic blood pressure over triptans alone.

The safety of ALD403 in combination with episodic use of triptans is critical for the patients that do not experience 100% reduction in their migraine days. The combination use of prophylaxis and abortive use of triptans as needed should significantly reduce the overall disease burden while minimizing safety/tolerability issues of triptan overuse.

### ALD403 Development Plans

Alder plans to start a dose ranging study with the ALD403 IV formulation in H2:14 in order to identify the optimal dose and dosing regimen to use in the pivotal Phase III study. The main endpoints in the study will be responder analysis (50%, 75% and 100% reduction of migraine days per month) and mean reduction in migraine days per month.

ALDR also plans to use information from the dose-ranging study to inform the design of the subcutaneous formulation study. ALDR will also conduct a Phase III in both episodic migraines and chronic migraine patients with both formulations, with the goal of gaining a broad indication for the prevention of migraines (in both episodic and chronic migraine patients).

ALDR also plans to better characterize the responders on a molecular level in future studies. They could measure serum CGRP, response to CGRP therapy following capsaicin treatment, other circulating markers, etc. The goal would be to prospectively identify patients who might benefit most from anti-CGRP.

## ALD403 Formulations

ALDR believes there is a need for both IV and subcutaneous formulations, separately or by combining the two, with an IV induction for rapid onset of action followed by long-term chronic subcutaneous therapy. Ideally, ALDR would like to be able to achieve a quarterly infusion regimen using the IV formulation.

ALDR estimates that the subcutaneous formulation has approximately 72% absolute bioavailability, suggesting that it will be an effective route of delivery.

## Breakthrough Therapy Designation

ALDR is considering filing for breakthrough therapy designation for ALD403. It is unclear how this application will be received, given most of the breakthrough therapy designations granted are for very severe or lethal conditions. Additionally, LLY also has data available that it could use for a filing, so we believe one or more companies could file for the designation for a therapy targeting CGRP biology in migraines.

## Marketing of ALD403

Patients with severe migraines are typically treated by headache specialists. ALDR estimates that the marketing can be done with a 75-100 person sales team, which will target neurologists and headache centers. We believe that most of the targeted specialists will be neurologists, who have broad experience with biologics for treating multiple sclerosis. Most of these physicians should have sufficient experience with using a biologic and the necessary infusion suite.

## Competitive Landscape

There are currently four antibodies in development for migraine prophylaxis that target the CGRP pathway.

- **Target:** The drugs from ALDR, LLY, and Labrys are most similar, all targeting soluble CGRP. AMGN's program is different and targets the CGRP receptor. This could provide unexpected benefits relative to the therapies targeting the ligand, but it could also cause unexpected side effects by affecting the biology of the receptor.
- **Data:** To date, we have only seen clinical efficacy results from ALDR and LLY, which were both featured at AAN in May 2014. Both drugs showed substantial reductions in key primary and secondary endpoints. These results provide significant derisking for the drug class.
- **Stage:** Both AMGN and Labrys have moved ahead of the pack with large Phase II trials in high-frequency episodic and chronic migraine. Neither company has established efficacy in prior studies, but both have selected doses or are advancing multiple doses in more definitive Phase II studies.

Exhibit 14: Competitive Landscape

Company	Drug	MOA	Stage
Alder	ALD403	Anti-CGRP	Phase II
Eli Lilly	LY2951742	Anti-CGRP	Phase II
Amgen	AMG 334	Anti-CGRP receptor	Phase II
Labrys	LBR-101/PFE-04427429	Anti-CGRP	Phase II

Source: Company data, Credit Suisse research.

**Exhibit 15: AMGN and Labrys Already in Large Phase II Programs****Labrys**

	LBR-101-022	LBR-101-021
Stage	Phase II	Phase II
# of patients	270	225
Indication	High frequency episodic migraine	Chronic migraine
Migraine days per month	8-14 migraine days/ month	≥15 migraine days/ month
Treatment arms	LBR-101 high and low dose vs. placebo	LBR-101 high and low dose vs. placebo
Dosing	Monthly subcutaneous	Monthly subcutaneous
Duration	12 weeks	12 weeks
Primary endpoint	Mean change in monthly migraine days	Mean change in headache hours
Start	Jan-14	Jan-14
Primary completion	Jan-15	Feb-15
Status	Enrolling	Enrolling
Identifier	NCT02025556	NCT02021773

**Amgen**

	20120178	20120295
Stage	Phase II	Phase II
# of patients	468	490
Indication	High frequency episodic migraine	Chronic migraine
Migraine days per month	4-14 migraine days/ month (past 3 months)	≥15 migraine days/ month
Treatment arms	AMG 334 (3 doses) vs. placebo	AMG 334 vs. placebo
Dosing	not disclosed	not disclosed
Duration	12 weeks	12 weeks
Primary endpoint	Change in monthly migraine days from baseline to last 4 weeks of 12 week dosing	Change in monthly migraine days from baseline to last 4 weeks of 12 week dosing
Secondary endpoints	50% responder analysis	50% responder analysis
Start	Aug-13	Feb-14
Primary completion	Aug-14	Feb-16
Status	Enrolling	Not yet enrolling
Identifier	NCT01952574	NCT02066415

Source: Company data, Credit Suisse estimates.

**Eli Lilly's LY2951742—Demonstrated Efficacy Across Multiple Endpoints**

LLY recently presented data from a randomized, double blind, placebo-controlled Phase II study (ART-01) with 218 patients with high frequency migraines (4-14 migraine days per month). These results were reported at AAN in May 2014, and we have reproduced the key data slides in Exhibit 16, Exhibit 17, Exhibit 18, and Exhibit 19.

Patients were dosed subcutaneously with 150 mg of LY2951742 every two weeks for 12 weeks. The average number of migraine days in the treated group was (6.7), which was lower than what ALDR reported for its treated patient population (8).

LY2951742 demonstrated clear efficacy by several measures including (1) reduction in migraine headache days at week 12 (-4.2 versus -3 for placebo) and a 50% responder analysis in month 3 (70.4% vs. 45.2% for placebo). It should be noted that this responder analysis was different from ALDR's. Responders in ALDR's trial had to respond in each of the three months of the study. A more apples-to-apples responder analysis comparison can be found in Exhibit 20.

The only substantial safety/tolerability signal in the LLY trial was injection site pain (16.8% versus 6.4%). The injection site pain may be due to the formulation (not known). In contrast, ALDR did not report any injection site pain.



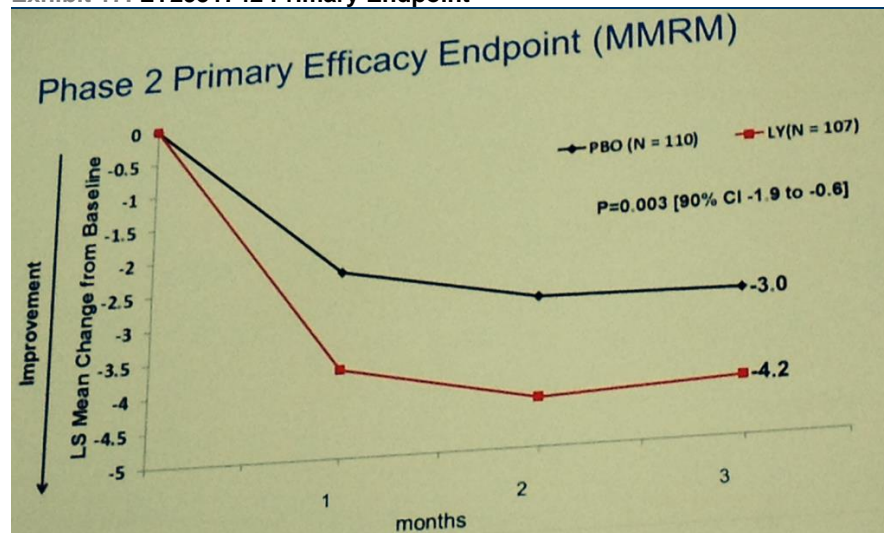
Our view is that both drugs appear safe and efficacious, lowering the risk for the entire new drug class. While it is very hard to compare the two datasets, ALDR's drug appears to be directionally better on some measure, most notably with the 100% reduction in migraine days. (See Exhibit 20—table of comparative efficacy).

Exhibit 16: LY2951742 Baseline Characteristics

Characteristic (mean value)	LY2951742 (N=107)	Placebo (N=110)
Migraine Headache Days (MHD) per month	6.7	7.0
Headache Days per month	8.6	9.1
Probable MHD, plus MHD per month	8.1	8.4
Migraine Attacks per month	4.9	5.0
Mean severity of Migraine Pain (1=mild, 2=moderate, 3=severe)	2.38	2.32
Aura	Yes	
	43%	40%

Source: LLY presentation at AAN 2014.

Exhibit 17: LY2951742 Primary Endpoint



Source: LLY presentation at AAN 2014.

Exhibit 18: LY2951742 Secondary Endpoints (1 of 2)

Mean change at month 3 when compared to baseline			
Secondary Endpoints	LY2951742	Placebo	P value
Change in Headache Days	-4.9	-3.7	P=0.0117 [90% CI -2.1 to -0.5]
Change in Migraine Attacks	-3.1	-2.3	P=0.0051 [90% CI -1.3 to -0.3]
Change in Migraine and Probable Migraine Headache Days	-4.8	-3.5	P=0.0101 [90% CI -2.2 to -0.5]

Source: LLY presentation at AAN 2014.

Exhibit 19: LY2951742 Secondary Endpoints (2 of 2)

Proportion of Responders: Responder is defined as a patient with a >50% reduction in Migraine Headache Days				
	LY2951742 n (%)	Placebo n (%)	Odds Ratio	90% CI
Month 1	62 (57.9)	41 (37.3)	2.40	1.51;3.81
Month 2	66 (66.0)	47 (44.3)	2.25	1.41;3.59
Month 3	69 (70.4)	47 (45.2)	2.88	1.78;4.69

Source: LLY presentation at AAN 2014.

Exhibit 20: Comparison of ALDR vs. LLY

	LY2951742	ALD403
# of pts	208	163
Dose and schedule	150mg subcutaneous every 2 weeks	1,000 mg intravenous once
Decrease in MHD	-4.2 (62.5%) vs. -3.0 (42%)	-5.6 (66%) vs. -4.6 (52%)
50% responder (month 1)	58% vs. 37%	75% vs. 50%
50% responder (month 2)	66% vs. 44%	76% vs. 54%
50% responder (month 3)	70% vs. 45%	75% vs. 67%
100% responder (month 3)	33% vs. 17%	41% vs. 16%
Injection site pain	17%	none reported

Source: AAN 2014.

# Clazakizumab—Bristol Deal Is a Winning Strategy for Alder

Clazakizumab is an antibody that targets IL-6 for the treatment of rheumatoid arthritis, psoriatic arthritis, and potentially other autoimmune/inflammatory diseases. ALDR partnered autoimmune indications for this product with Bristol, in a deal that we believe maximizes the value of the asset for ALDR, while minimizing financial risk.

Before we describe clazakizumab, its clinical data, and the emerging roll of IL-6 inhibitors, it is worth noting some of the key features of the Bristol deal.

- **Ideal Partner:** Bristol is already a player in the RA and autoimmune space, although it is far from a leader. In RA, Bristol markets Orencia (abatacept, CTLA4-Ig), which is generally viewed as a second/third line biologic. The fact that Bristol does not already have a first-line anti-TNF agent provides the partner with maximum motivation to aggressively position Clazakizumab as an alternative to anti-TNF agents. Bristol is also developing Eldelumab (anti-IP10) in Phase II for Crohn's disease. Bristol is a major force in antibody development and therefore also brings expertise in formulation, manufacturing, and other non-clinical aspects of development.
- **No Development Expenses for ALDR:** At the time the deal was signed in 2009, ALDR was a private company with uncertain access to capital. The deal was structured to require no capital outlay by ALDR for the development of clazakizumab in RA and autoimmune disease. This is a critical part of the value, in our view. The cost of developing a new RA drug is high, and the market is getting increasingly crowded and complex. The bottom line is that the return on invested R&D dollars may be lower, favoring a more passive out-licensing strategy for a small biotech company.
- **Lucrative Milestone Structure Funds Proprietary Pipeline:** Many biotech deals use milestones as a form of paid development costs, in which the milestone payments are designed to offset a cost-sharing arrangement (e.g., the PCYC/JNJ deal). For ALDR, the cash payments do not have an offsetting development expense obligation and can therefore be used to fund proprietary development of other programs such as ALD403. The deal included \$85M upfront, \$18.5M in earned milestones to date, \$746M in remaining development and regulatory milestones (pre-commercial), and \$500M in sales milestones. Of the \$746M in development and regulatory milestones, \$348M is associated with the RA program and is very likely to be achieved, in our view. We believe the \$348M is spread across Phase III development and regulatory progress (filing and approval) in three different territories.
- **Midteen to 20% Royalty:** Given the likely high marketing costs associated with launching a new RA drug, we believe a royalty structure is the best outcome. A profit share would transfer significant cost burden to ALDR and delay cash flow. The royalty rate is on the high side considering the deal was done back in 2009 without significant clinical data.
- **Valuation Is Heavily Weighted Toward Near-Term Milestones:** Our current valuation includes \$4/share for clazakizumab. This consists of ~\$1.60/share for the pre-commercial milestones in RA, ~\$1.20/share for milestones in other indications, and ~\$1.20/share for the royalty and sales milestones. This royalty portion is highly dependent on the commercial success of the product, while the RA milestones are much higher probability, in our view.

Motivated to compete in early lines of treatment

70% of the value of the program is in the milestones according to our DCF

**Exhibit 21: Terms of the Bristol Clazakizumab Deal**

Partner	Bristol-Myers Squibb
Product/scope	Clazakizumab
Date:	November 2009
<b>Terms:</b>	
Upfront payment	\$85M
Milestones (paid)	\$18.5M
Milestones (future)	~\$350M (RA Development) ~\$400M (Two other indications) \$500M (Sales) - all indications
Royalties	Tiered mid-teen to twenty percent in royalties on WW net sales
<b>Bristol responsibilities:</b>	
Territories	Global
Expenses	100% of development, regulatory, and commercial expenses

Source: Company data, Credit Suisse research.

## Rheumatoid Arthritis Is Crowded, but Clazakizumab Will Likely Find Its Place in Second Line

The current biologic market in RA and autoimmune diseases is approximately \$18 billion in the U.S. alone. In RA, patients typically start treatment on a variety of cheap generic drugs that are classified as disease-modifying anti-rheumatoid drugs (DMARDs), including methotrexate. Following an inadequate response to standard DMARDs, patients may receive any of a number of injectable biologics, most commonly anti-TNF agents. The market-leading anti-TNF agents are Humira (ABBV), Enbrel (AMGN), and Remicade (JNJ).

After an inadequate response to a first-line anti-TNF agent, the choices become more complex. Patients often switch to another anti-TNF agent or switch drug classes. Other drugs and drug classes may include:

- New oral JAK inhibitors (e.g., PFE's Xeljanz)
- Anti-IL6R (Roche's Actemra)
- CTLA4-Ig (Bristol's Orencia)
- Anti-CD20 (Roche's Rituxan)

The space is getting increasingly complex, with more competition coming from within existing drug classes (e.g., multiple new anti-IL6R and anti-IL6 antibodies) and new drug classes including new oral agents. In the longer-term, the RA market is likely to experience the introduction of biosimilars, particularly biosimilar anti-TNF agents. Both of these factors are negative headwinds for any new biologic.

While many companies are running head-to-head trials versus anti-TNF agents, the likelihood of displacing anti-TNFs as the go-to first-line biologic is very low, given the long clinical history and good safety/efficacy profile. The best opportunity for new agents is to become high on the list of alternative agents for patients who do not adequately respond to their first biologic.

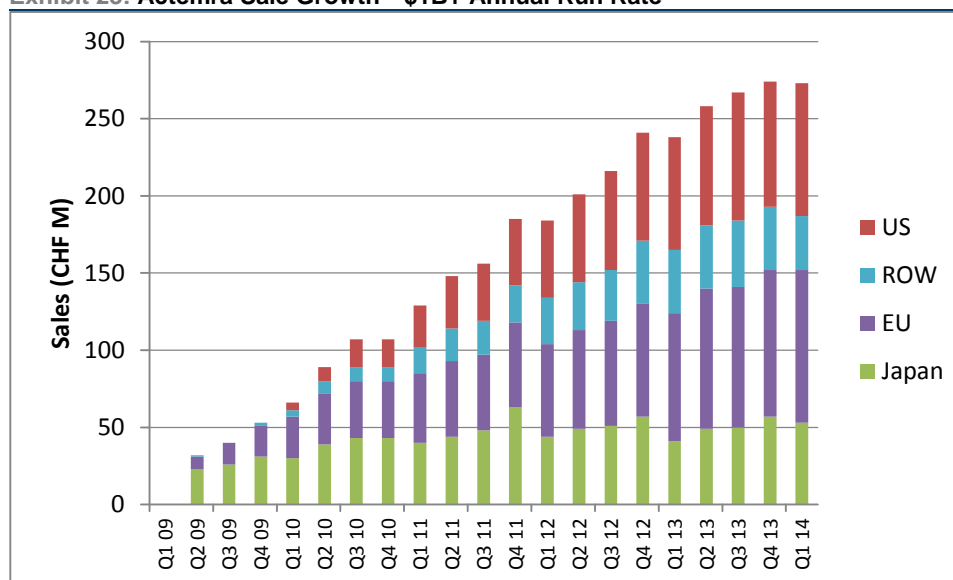
**Exhibit 22: Select Drug Classes in Development for RA/PsA**

Trade name	Other name(s)	Company	Target	Modality	Status in RA or PsA
Humira	Adalimumab	ABBV	Anti-TNF	Antibody	Approved
Enbrel	Etanercept	AMGN	Anti-TNF	Receptor fusion	Approved
Remicade	Infliximab	JNJ	Anti-TNF	Antibody	Approved
Simponi	Golimumab	JNJ	Anti-TNF	Antibody	Approved
Cimzia	Certolizumab pegol	UCB	Anti-TNF	PEGylated Fab'	Approved
Actemra	Tocilizumab	ROG.X	Anti-IL6R	Antibody	Approved
	Sarilumab	REGN / SASY	Anti-IL6R	Antibody	Phase III
	Sirukumab (CNTO136)	JNJ	Anti-IL-6	Antibody	Phase III
	Clazakizumab (BMS-945429)	BMJ / ALDR	Anti IL-6	Antibody	Phase IIb
	ALX-0061	ABBV / Ablynx	Anti-IL6R	Nanobody	Phase IIa
Rituxan	Rituximab	Roche	Anti-CD20	Antibody	Approved
Xeljanz	tofacitinib citrate	Pfizer	JAK inhibitor	Small molecule	Approved
	Baricitinib (LY3009104, INCB28050)	LLY / INCY	JAK inhibitor	Small molecule	Phase III
	ABT-494	ABBV	JAK inhibitor	small molecule	Phase II
	GLPG0634	ABBV / GLPG	JAK inhibitor	small molecule	Phase II
	VX-509	Vertex	JAK inhibitor		Phase II
Orencia	Abatacept	BMJ	CTLA4-Ig	Fusion protein	Approved
	Secukinumab (AIN457)	NVS	Anti-IL-17	Antibody	Phase III
	Ixekizumab (LY2439821)	LLY	Anti-IL-17	Antibody	Phase III

Source: Company data, Credit Suisse research.

### Opportunity for Anti-IL6 Based Therapies

The flagship product in this drug class is Roche's Actemra, an anti-IL6 receptor antibody. The uptake of this drug was initially slow due primarily to its IV formulation and lack of comparative data. Subsequently, Roche has launched a new subcutaneous formulation (October 2013) and generated favorable Phase III head-to-head data comparing monotherapy Actemra with monotherapy Humira. The result is a growing franchise with over \$1b in annualized worldwide sales (CHF 273M in Q1:14, up 23% y/y).

**Exhibit 23: Actemra Sale Growth—\$1B+ Annual Run Rate**

Source: Company data, Credit Suisse research.

A steady, growing product for Roche and a market that is primed for new entrants



## Growing Number of Anti-IL6 Antibodies

In addition to Actemra, there are at least two other antibodies in development targeting the IL-6 receptor and three other antibodies targeting the ligand IL-6. In general, the activity of IL-6 targeted antibodies has demonstrated consistent positive efficacy and similar safety profiles. As a result, we believe the success of individual agents will largely be determined by the growth of the IL-6 class, which will also be helped by the increased clinical data and marketing efforts generated by new entrants.

- **Sarilumab:** Sanofi and Regeneron have ongoing Phase III trials for sarilumab in RA. The Phase III MOBILITY trial already demonstrated positive results, largely derisking the program. Sarilumab is most similar to Actemra (targets the receptor), and it is formulated as a convenient subcutaneous injection.
- **Sirukumab:** JNJ's Centocor division developed an anti-IL6 antibody that is in Phase III development for RA. This drug is the most similar to clazakizumab (both target the ligand). Like clazakizumab, sirukumab is also formulated as a subcutaneous injection.

### Exhibit 24: IL6 Targeted Therapies

Drug	Company	Description	Target(s)	Stage	Route	Indication
Actemra	Roche	Antibody	IL-6R	Marketed	IV and SC	RA
Sarilumab	Regeneron / Sanofi	Antibody	IL-6R	Phase III	SC	RA
ALX-0061	Ablynx / Abbvie	Nanobody	IL-6R	Phase IIa	IV and SC	RA, SLE
CNT0136 (sirukumab)	Centocor	Antibody	IL-6	Phase III	SC	RA
BMS-945429 (Clazakizumab)	Alder / Bristol	Antibody	IL-6	Phase IIb		RA

Source: Company data, Credit Suisse estimates

## Positive Clinical Efficacy for Clazakizumab

Bristol ran a large seven-arm Phase II trial testing three different monthly doses of clazakizumab with or without methotrexate (MTX) versus MTX alone or the standard-of-care combination of Humira plus MTX. (See Exhibit 25.) The primary efficacy results at 12 weeks were positive and presented at ACR 2013.

The three major efficacy conclusions from the primary analysis are as follows.

- **Monotherapy with Clazakizumab Compared Favorably with Standard of Care Humira + MTX (see Exhibit 26):** Results trended better for clazakizumab on the stringent ACR70 score and trended slightly worse on ACR20 and ACR50.
- **Clazakizumab + MTX Beats Humira + MTX on Stringent ACR70 Score (see Exhibit 27):** While ACR20 and ACR50 were similar, ACR70 showed a clear advantage for clazakizumab at all three doses tested.
- **Clazakizumab + MTX Showed Superior Remission Rates (see Exhibit 28):** Both by DAS28 and CDAI scores, clazakizumab + MTX was superior to placebo or Humira.

On the safety side, clazakizumab was associated with (1) modest elevations in liver enzymes, (2) modest increases in cholesterol, and (3) higher infection rates. (See Exhibit 31.) These side effects have been seen with other IL-6 targeted agents. There was no detectable immunogenicity.

Overall, these results support a move into larger confirmatory trials. One of the key open questions is the lowest effective dose. In this trial, all three dose groups performed well versus placebo and Humira, and Bristol needs to further evaluate the bottom end of the dose response curve.

On stringent efficacy measures, clazakizumab beats Humira

Increased laboratory abnormalities and infections may limit the growth of IL-6 inhibitors versus TNF inhibitors

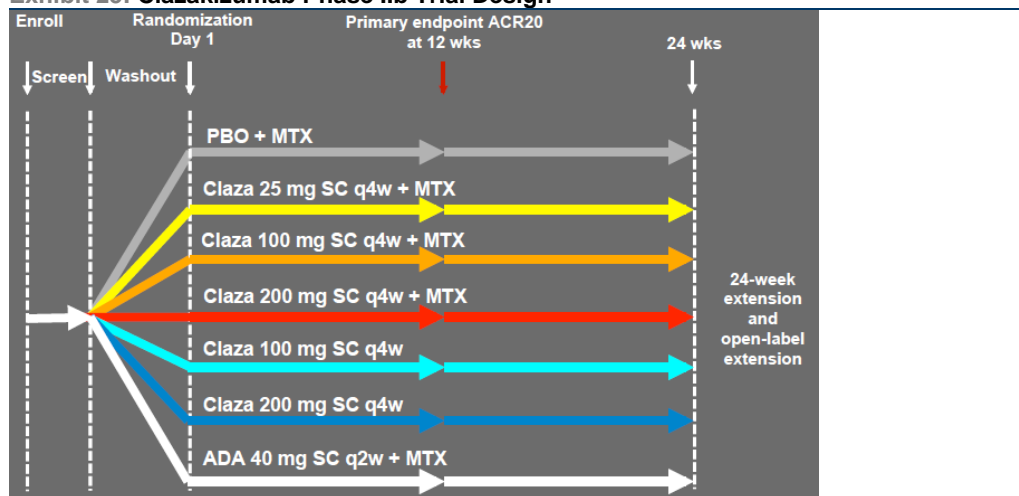


### Additional Data Presentations for Clazakizumab at EULAR

Bristol will present updated data at EULAR on June 14 from the previously reported Phase IIb trial in RA. New data will include 24-week results (prior data was 12 weeks), X-Ray and MRI results at weeks 12 and 24 (see Exhibit 29), and patient-reported outcomes (see Exhibit 30). Data are already available in the abstracts, and they are consistent with the previously reported results. Clazakizumab + MTX performs universally better than placebo + MTX. Compared with Humira, the results are more variable than the 12-week symptom data. In general, clazakizumab is comparable with Humira by these measures, with more variability in the outcome measures. Data presentations include:

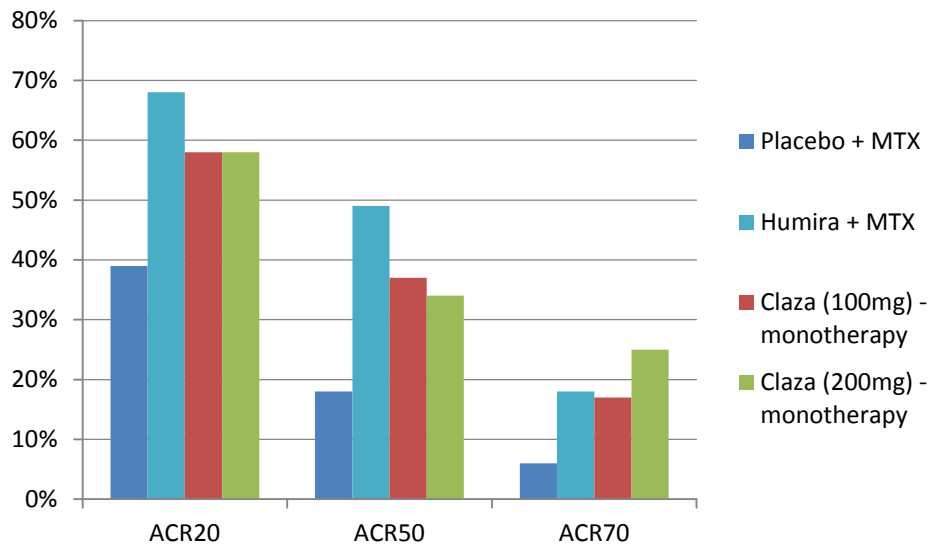
- A Phase IIB Study of the Efficacy and Safety of Subcutaneous Clazakizumab (Anti-IL-6 Monoclonal Antibody) with or without Methotrexate in Adults with Moderate-to-Severe Active Rheumatoid Arthritis and an Inadequate Response to Methotrexate (June 14, 2014 at 10:15 a.m. CET)
- X-Ray and MRI Results from a Phase IIB Study of Subcutaneous Anti-interleukin-6 Monoclonal Antibody Clazakizumab with or without MTX in Adults with Moderate-to-Severe Active Rheumatoid Arthritis and an Inadequate Response to Conventional DMARDS Including Methotrexate (June 14, 2014 at 10:15 a.m. CET)

**Exhibit 25: Clazakizumab Phase IIb Trial Design**



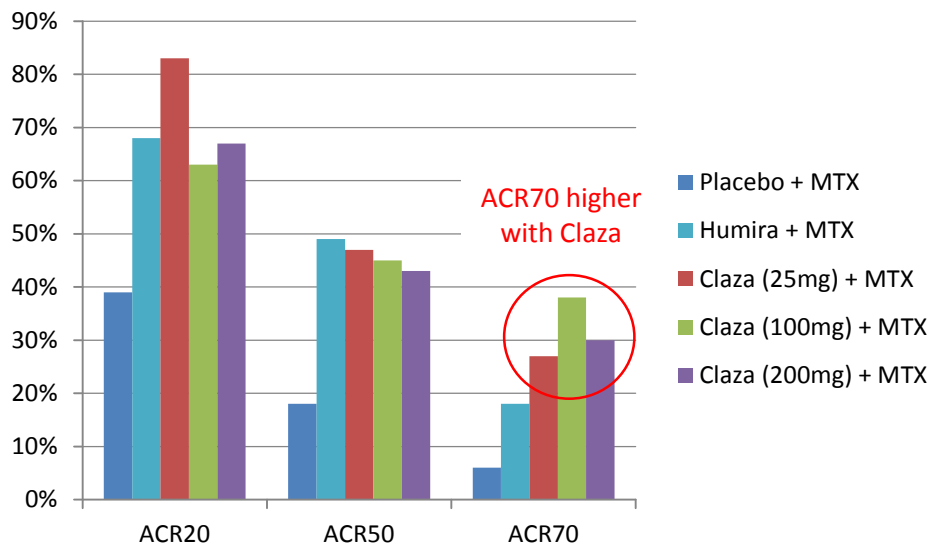
Source: ACR 2013.

**Exhibit 26: Favorable Comparison of Monotherapy with Humira + MTX**

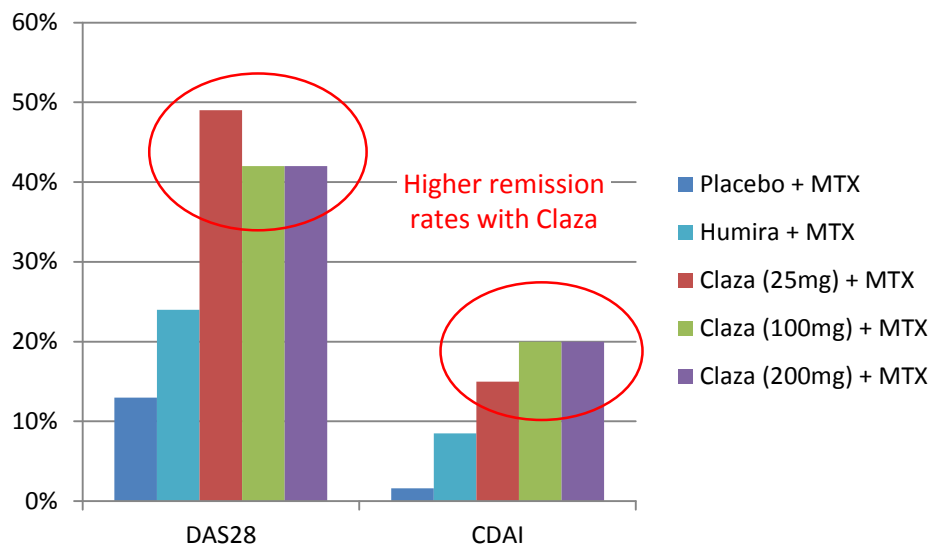


Source: ACR 2013.

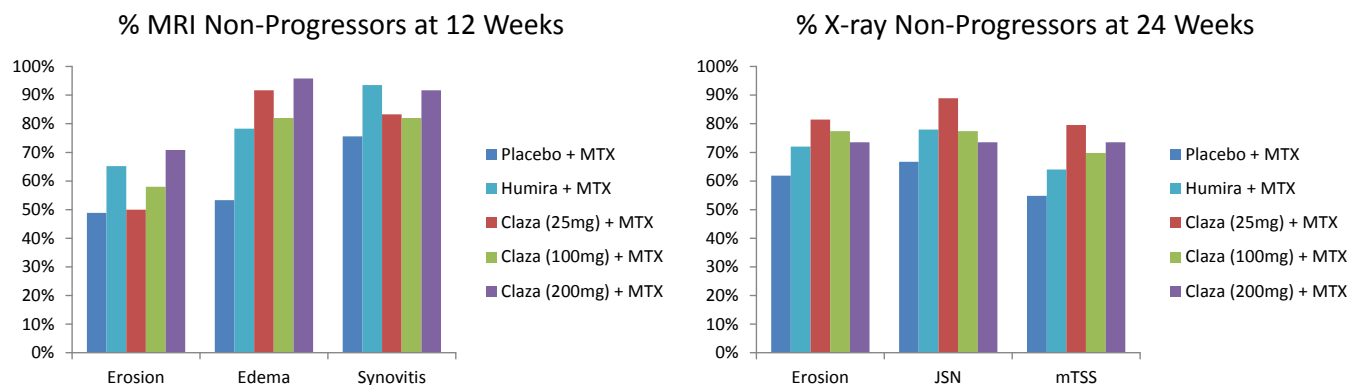
**Exhibit 27: Favorable Comparison with Standard of Care (both with MTX)**



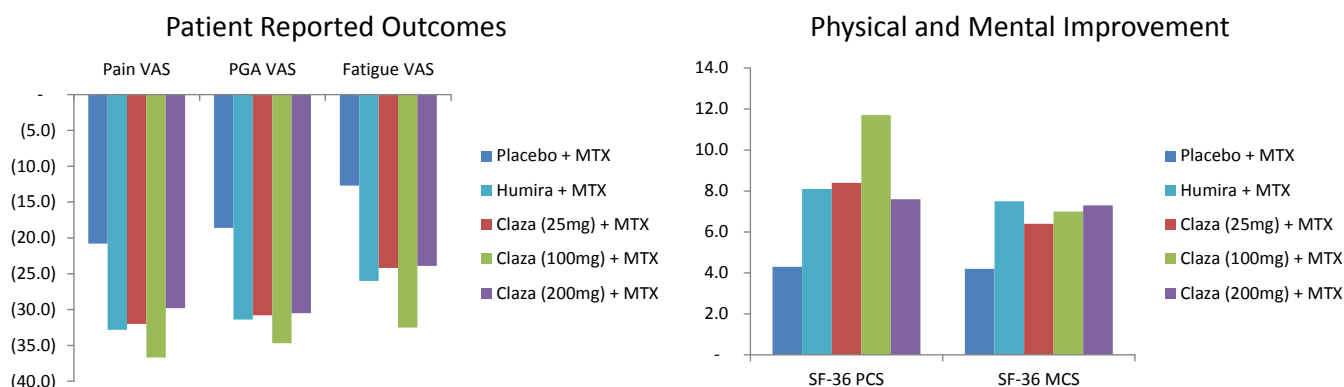
Source: ACR 2013.

**Exhibit 28: Better Remission Rates with Clazakizumab**

Source: ACR 2013.

**Exhibit 29: Clazakizumab X-Ray and MRI Results—More Variable but Similar to Humira**

Source: EULAR 2014 abstracts.

**Exhibit 30: Patient Reported Outcome Measures Similar to Humira**

Source: EULAR 2014 abstracts.

**Exhibit 31: Safety Analysis of Phase IIb Data**

Week 24	Placebo + MTX	Clazakizumab monotherapy		Clazakizumab + MTX			Humira + MTX
		100mg Q4 week	200mg Q4 week	25mg Q4 week	100mg Q4 week	200mg Q4 week	
# of pts	61	60	59	59	60	60	59
SAEs	3.3%	8.3%	13.6%	8.5%	8.3%	8.3%	5.1%
Disc for SAE	0.0%	1.7%	3.4%	0.0%	5.0%	0.0%	0.0%
AEs	59.0%	88.3%	86.4%	83.1%	96.7%	90.0%	74.6%
Infections	0.0%	1.7%	5.1%	3.4%	5.0%	5.0%	3.4%
Malignancies	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
Lab abnormalities	0.0%	1.7%	0.0%	0.0%	1.7%	0.0%	0.0%
ALT*	n=51	n=55	n=53	n=54	n=54	n=53	n=47
>1-3 ULN	21.6%	38.2%	50.9%	46.3%	44.4%	56.6%	23.4%
>3-5 ULN	2.0%	1.8%	0.0%	3.7%	13.0%	17.0%	0.0%
>5-8 ULN	0.0%	0.0%	0.0%	3.7%	1.9%	3.8%	0.0%
AST*	n=54	n=57	n=56	n=55	n=53	n=58	n=51
>1-3 ULN	14.8%	19.3%	37.5%	40.0%	47.2%	62.1%	23.5%
>3-5 ULN	0.0%	0.0%	0.0%	3.6%	3.8%	3.4%	0.0%
>5-8 ULN	0.0%	1.8%	0.0%	0.0%	0.0%	0.0%	0.0%
Bilirubin*	n=55	n=58	n=56	n=57	n=59	n=58	n=55
>1.0-1.5 ULN	0.0%	5.2%	8.9%	8.8%	14.0%	6.8%	0.0%
>1.5-2.0 ULN	0.0%	1.7%	8.9%	1.8%	3.5%	3.4%	1.8%
>2.0-3.0 ULN	0.0%	1.7%	0.0%	0.0%	0.0%	1.7%	0.0%
LDL*	n=46	n=41	n=41	n=42	n=44	n=48	n=46
LDL >130 mg/dL	28%	66%	61%	62%	59%	52%	39%

Source: ACR 2013.

**Ongoing Clinical Trials of Clazakizumab—Phase IIb in RA**

Following the positive results of the first Phase IIb, Bristol embarked on a study to more fully explore the lower end of the dose response curve prior to choosing a Phase III dose. The current ongoing study includes three doses of clazakizumab (1mg, 5mg, and 25mg) + MTX versus placebo + MTX for 12 weeks. The trial will enroll approximately 140 patients with inadequate response to TNF inhibitors. The trial also includes a 96-week long-term treatment phase.

The primary endpoint of the trial is the DAS28-CRP score, and secondary endpoints include a variety of efficacy measures including ACR20/50/70, CDAI, quality of life, and others.

Bristol will use this Phase IIb and the results of the prior Phase IIb to design a Phase III program, which should begin in H1:15.

**Ongoing Clinical Trials of Clazakizumab—Phase II in Psoriatic Arthritis**

Bristol expects to report results in 2014 from a Phase II trial of clazakizumab versus placebo in the treatment of psoriatic arthritis. The trial is fully enrolled, with 150 patients on a stable background of MTX. Patients are included if they are inadequate responders to NSAIDs or non-biologic DMARDs, and patients may not have had a previous biologic therapy.

The trial randomized patients to one of three doses of monthly clazakizumab (25mg, 100mg, and 200mg) versus placebo. The primary endpoint is ACR20, and important secondary endpoints include PASI75, ACR50/70, quality of life, and others.

Results from this study and the complete Phase IIb program in RA are likely to inform the design of a Phase III trial in psoriatic arthritis.

# Productive Antibody Platform

ALDR has built a suite of antibody technologies spanning initial antibody generation and selection through to manufacturing. There are advantages to its approach at every step, although the true value of the platform is best judged by its productivity, which includes two clinically validated therapeutic antibody candidates (clazakizumab and ALD403). Both have high potency, good half-life, low/no immunogenicity, and high-yield manufacturing.

We believe this platform will continue to be a source of value, measured by the generation of new clinical candidates for proprietary development and potentially for out-licensing. ALDR is currently evaluating four preclinical programs and plans to advance at least one candidate into the clinic in 2015.

- **Antibody Generation:** The key differentiator for ALDR is that the initial antibodies are generated in rabbits. Most other processes involve starting with genetically engineered or native mice. ALDR is able to efficiently humanize antibodies from rabbits.
- **Antibody Selection:** Using its ABS technology, ALDR is able to select for antibodies that are high affinity and have the desired properties: specificity, target antagonism, formulation properties, etc. The best evidence of the success of this process is the two current clinical candidates which are very well behaved antibodies.
- **Antibody Production:** The MAbXpress system is perhaps the most differentiated part of ALDR's technology platform and the one that can most easily be described relative to standard approaches. ALDR produces its antibodies in *Pichia* yeast rather than traditional CHO cells (Chinese hamster ovary). There are several advantages to this system, which all contribute to a potentially very low cost of goods, including: (1) proprietary, with no royalties or licenses required, (2) very high yield, (3) relatively short production time, and (4) less expensive raw materials.

The *Pichia* production system does not glycosylate the antibodies. This may have certain advantages related to immunogenicity and half-life. However, lack of glycosylation may limit the applications of the technology in certain situations. For example, many of the antibodies approved for treating cancer utilize immune cell activation as part of their mechanism of action. Some of these features are enhanced by certain glycosylations on the antibody.

**Exhibit 32: Potential Cost Advantages of MabXpress**

	Conventional cell culture	Alder's MabXpress
Cost	\$300-1,000/g	<\$100/g
Royalties	15-20%	0%
Capacity	Limited	Available
Tank sizes	12,000 or 20,000 L	Scale to 160,000 L
Development time	Years	Months

Source: Company data, Credit Suisse estimates.

**Exhibit 33: Potential Time Savings with MabXpress**

	Typical CHO	ALD403
Cell bank mfg/release	6-9 months	1 month
Process development	12 months	5 months
Process transfer	2 months	2 months
Drug manufacture	3 months	1 month
Test and release	3 months	1 month
Total	26 months	10 months

Source: Company data, Credit Suisse estimates.

# ALDR Management

The team at ALDR includes founding members with significant experience in protein/antibody engineering and drug development. Many of them worked together at Celltech.

- **Randall C. Schatzman, Ph.D.**—Dr. Schatzman has served as president, chief executive officer, and director since he co-founded ALDR, in January 2004. From 1999 to 2004, he served as senior vice president of discovery research at Celltech. From 1995 to 1999, he served as director of gene discovery at Mercator Genetics Inc., a genomics company. From 1987 to 1995, he served as section leader at Roche Bioscience, previously Syntex Corp., where he helped found the Cancer and Developmental Biology Institute. Dr. Schatzman holds a Ph.D. in Molecular Pharmacology from Emory University and a B.S. in biochemistry from Purdue.
- **John A. Latham, Ph.D.**—Dr. Latham has served as chief scientific officer since he co-founded the company in January 2004. From 1998 to 2004, he served as a director, senior director, and most recently as vice president of gene function and target validation for Celltech Group plc. In 1994, he joined Darwin Molecular Corporation, a first-generation gene-to-drug biotechnology company as a founding director, where he served from 1994 to 1998. He was one of the early scientists hired by Gilead Sciences, and from 1989 to 1994, he was a member of a core group established to exploit novel oligonucleotide-based technologies. Dr. Latham holds a Ph.D. in Biochemistry from Massachusetts Institute of Technology and a B.S. in chemistry from Colorado State University.
- **Mark J. Litton, Ph.D.**—Dr. Litton has served as chief business officer, treasurer and secretary since he co-founded the company in January 2004. From 1999 to 2004, he served as vice president of business development for Celltech Group, where he was responsible for securing, commercializing, and partnering numerous novel discoveries and therapeutic opportunities. From 1997 to 1999, he served as the manager of business development for Ribozyne Pharmaceuticals Inc., currently Sirna Therapeutics, Inc., where he helped form relationships with Eli Lilly and Company, Roche Bioscience, and GlaxoWellcome. Dr. Litton holds a Ph.D. in immunology from Stockholm University, an M.B.A. from Santa Clara University, and a B.S. in biochemistry from the University of California, Santa Cruz.
- **Jeffrey T.L. Smith, M.D., FRCP**—Dr. Smith has served as senior vice president, translational medicine since 2012 and served in other senior management positions from April 2004 to 2012. From 1999 to 2004, he served as senior director of medical research for Celltech R&D, where he was responsible for planning and managing the CDP870 anti-TNF clinical trials for RA as well as several other key autoimmune clinical development programs. From 1997 to 1999, he served as medical director at Simbec Research, a contract research organization. From 1995 to 1997, he served as head of clinical pharmacology at Hoechst Marion Roussel. Before that, he held various positions at Proctor and Gamble from 1994 to 1995 and at Glaxo Research and Development from 1989 to 1994. Dr. Smith holds an M.D. from the University of London and is a Fellow of the Royal College of Physicians in London.
- **Larry K. Benedict**—Mr. Benedict has served as senior vice president of finance since January 2013 and prior to that served as vice president of finance since June 2008. From 2000 to 2008, he served in various positions at Seattle Genetics, most recently as director of finance and controller. He served as chief financial officer at Sensible Solutions from 1998 to 2000 and as finance manager at SmithKline Beecham Clinical Laboratories, now Quest Diagnostics Incorporated from 1997 to 1998. From 1990 to 1997, he held various finance roles at Bristol-Myers Squibb Company, a biopharmaceutical company. Mr. Benedict holds a B.S. in accounting from Central Washington University.



# Financial Statements

**Exhibit 34: Income Statement**

	2012A	2013A	Q1:14E	Q2:14E	Q3:14E	Q4:14E	2014E	2015E	2016E	2017E	2018E	2019E
<b>Revenues</b>												
US sales of ALD403												29.7
Ex-US royalties on ALD403												2.4
Royalties on Clazakizumab												197.6
Collaboration and license agreement	20.1	18.8	4.7	4.7	4.7	4.7	18.7	59.3	25.3	7.5	103.1	
<b>Total Revenues</b>	<b>20.1</b>	<b>18.8</b>	<b>4.7</b>	<b>4.7</b>	<b>4.7</b>	<b>4.7</b>	<b>18.7</b>	<b>59.3</b>	<b>25.3</b>	<b>7.5</b>	<b>103.1</b>	<b>229.7</b>
<b>Expenses</b>												
Cost of goods												3.0
Research and development	30.7	31.9	6.5	8.0	10.0	12.0	36.5	58.5	74.0	90.0	92.0	87.0
Sales, general, administrative	7.2	7.7	2.0	3.0	3.5	4.0	12.5	21.0	24.0	24.0	26.0	35.0
<b>Total Operating Expenses</b>	<b>37.9</b>	<b>39.6</b>	<b>8.5</b>	<b>11.0</b>	<b>13.5</b>	<b>16.0</b>	<b>49.0</b>	<b>79.5</b>	<b>98.0</b>	<b>114.0</b>	<b>118.0</b>	<b>122.0</b>
Operating income (loss)	(17.8)	(20.8)	(3.8)	(6.3)	(8.8)	(11.3)	(30.3)	(20.2)	(72.7)	(106.5)	(14.9)	107.7
Total Other Income (Expense)	0.0	0.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.2	0.2
Pre Tax Income	(17.8)	(20.6)	(3.8)	(6.3)	(8.8)	(11.3)	(30.2)	(20.2)	(72.7)	(106.5)	(14.7)	107.9
Income tax												
<b>Net Income</b>	<b>(17.8)</b>	<b>(20.6)</b>	<b>(3.8)</b>	<b>(6.3)</b>	<b>(8.8)</b>	<b>(11.3)</b>	<b>(30.2)</b>	<b>(20.2)</b>	<b>(72.7)</b>	<b>(106.5)</b>	<b>(14.7)</b>	<b>107.9</b>
EPS - diluted (proforma)	(\$3.55)	(\$3.84)	(\$0.65)	(\$0.24)	(\$0.28)	(\$0.36)	(\$1.10)	(\$0.60)	(\$1.85)	(\$2.26)	(\$0.31)	\$2.09
Shares outstanding - basic (proforma)	5.01	21.89	21.89	26.33	31.04	31.20	27.61	33.34	39.31	47.16	47.99	48.47
Shares outstanding - diluted (proforma)	5.01	21.89	21.89	26.33	31.04	31.20	27.61	33.34	39.31	47.16	50.97	51.60

Source: Company data, Credit Suisse estimates.

**Exhibit 35: Condensed Balance Sheet**

<b>Balance sheet</b>	2012A	2013A	2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E
<b>TOTAL ASSETS</b>	\$64.7	\$26.7	\$62.0	\$187.1	\$93.2	\$180.6	\$165.0	\$272.6	\$386.2	\$562.8
Total Current Liabilities	\$22.6	\$23.1	\$23.1	\$23.1	\$14.4	\$14.4	\$10.4	\$4.4	\$4.4	\$4.4
Total Liabilities	\$76.7	\$58.7	\$40.0	\$52.2	\$26.9	\$19.4	\$11.9	\$4.4	\$4.4	\$4.4
Convertible preferred stock	\$111.4	\$111.4								
Additional paid-in capital	\$1.8	\$2.4	\$198.1	\$331.1	\$335.2	\$536.5	\$543.2	\$550.4	\$558.5	\$567.3
Accumulated deficit	(\$125.2)	(\$145.8)	(\$176.1)	(\$196.2)	(\$268.9)	(\$375.3)	(\$390.0)	(\$282.2)	(\$176.6)	(\$8.8)
Total stockholders' deficit & liabilities	\$64.7	\$26.7	\$62.0	\$187.1	\$93.2	\$180.6	\$165.0	\$272.6	\$386.2	\$562.8

Source: Company data, Credit Suisse estimates.

**Exhibit 36: Condensed Cash Flow Statement**

<b>Cash Flow Statement</b>	2012A	2013A	2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E
Cash flow from operations	(\$19.5)	(\$36.1)	(\$46.3)	(\$4.2)	(\$92.8)	(\$106.9)	(\$14.6)	\$108.6	\$114.6	\$177.6
Cash flow from investing	(\$1.2)	\$5.5	(\$0.8)	(\$0.8)	(\$0.8)	(\$0.8)	(\$1.0)	(\$1.0)	(\$1.0)	(\$1.0)
Cash flow from financing		\$0.0	\$82.5	\$130.2		\$195.3				
Net Cash Increase (Decrease)	(\$20.7)	(\$30.5)	\$35.5	\$125.2	(\$93.6)	\$87.6	(\$15.6)	\$107.6	\$113.6	\$176.6
Beginning Cash	\$14.5	\$53.8	\$23.2	\$58.7	\$184.0	\$90.3	\$177.9	\$162.3	\$269.9	\$383.5
Ending Cash	(\$6.1)	\$23.2	\$58.7	\$184.0	\$90.3	\$177.9	\$162.3	\$269.9	\$383.5	\$560.1

Source: Company data, Credit Suisse estimates.

## Companies Mentioned (Price as of 30-May-2014)

**AbbVie Inc.** (ABBV.N, \$54.33)  
**Ablynx** (ABIX.BR, €8.863)  
**Alder Biopharmaceuticals** (ALDR.OQ, \$10.74, OUTPERFORM[V], TP \$20.0)  
**Alexion Pharmaceuticals Inc.** (ALXN.OQ, \$166.32)  
**Amgen Inc.** (AMGN.OQ, \$115.99)  
**Bristol Myers Squibb Co.** (BMY.N, \$49.74, OUTPERFORM, TP \$59.0)  
**Celldex** (CLDX.OQ, \$14.61)  
**Eli Lilly & Co.** (LLY.N, \$59.86)  
**Five Prime** (FPRX.OQ, \$12.99)  
**ImmunoGen, Inc.** (IMGN.OQ, \$11.82)  
**Incyte** (INCY.OQ, \$49.55)  
**Johnson & Johnson** (JNJ.N, \$101.46)  
**MacroGenics** (MGNX.OQ, \$18.66)  
**OncoMed** (OMED.OQ, \$22.6)  
**Regeneron Pharmaceutical** (REGN.OQ, \$306.96)  
**Roche** (ROG.VX, SFr263.5)  
**Sanofi** (SASY.PA, €78.44)  
**Seattle Genetics** (SGEN.OQ, \$33.37)  
**UCB** (UCB.BR, €58.48)  
**Vertex Pharmaceuticals Inc.** (VRTX.OQ, \$72.26)  
**XOMA Corporation** (XOMA.OQ, \$4.14)  
**Xencor, Inc** (XNCR.OQ, \$8.8)

## Disclosure Appendix

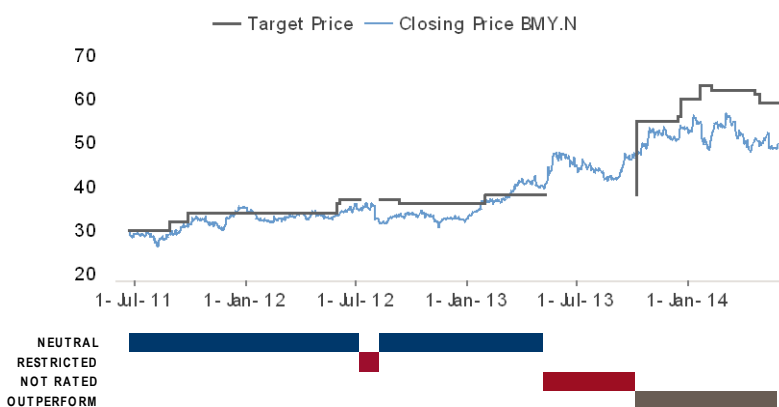
### Important Global Disclosures

I, Jason Kantor, PhD, certify that (1) the views expressed in this report accurately reflect my personal views about all of the subject companies and securities and (2) no part of my compensation was, is or will be directly or indirectly related to the specific recommendations or views expressed in this report.

### 3-Year Price and Rating History for Bristol Myers Squibb Co. (BMY.N)

BMY.N	Closing Price	Target Price	
Date	(US\$)	(US\$)	Rating
23-Jun-11	29.33	30.00	N
29-Aug-11	29.29	32.00	
27-Sep-11	31.24	34.00	
30-May-12	33.48	36.00	
04-Jun-12	33.66	37.00	
08-Jul-12	34.61		R
10-Aug-12	31.73	37.00	N
11-Sep-12	33.56	36.00	
31-Jan-13	36.14	38.00	
10-May-13	40.49		NR
08-Oct-13	46.60	55.00	O *
16-Dec-13	50.88	56.00	
20-Dec-13	53.37	60.00	
21-Jan-14	54.59	63.00	
09-Feb-14	50.33	62.00	
21-Apr-14	50.51	61.00	
30-Apr-14	50.09	59.00	

\* Asterisk signifies initiation or assumption of coverage.



The analyst(s) responsible for preparing this research report received Compensation that is based upon various factors including Credit Suisse's total revenues, a portion of which are generated by Credit Suisse's investment banking activities

### As of December 10, 2012 Analysts' stock rating are defined as follows:

**Outperform (O) :** The stock's total return is expected to outperform the relevant benchmark\* over the next 12 months.

**Neutral (N) :** The stock's total return is expected to be in line with the relevant benchmark\* over the next 12 months.

**Underperform (U) :** The stock's total return is expected to underperform the relevant benchmark\* over the next 12 months.

\*Relevant benchmark by region: As of 10th December 2012, Japanese ratings are based on a stock's total return relative to the analyst's coverage universe which consists of all companies covered by the analyst within the relevant sector, with Outperforms representing the most attractive, Neutrals the less attractive, and Underperforms the least attractive investment opportunities. As of 2nd October 2012, U.S. and Canadian as well as European ratings are based on a stock's total return relative to the analyst's coverage universe which consists of all companies covered by the analyst within the relevant sector, with Outperforms representing the

most attractive, Neutrals the less attractive, and Underperforms the least attractive investment opportunities. For Latin American and non-Japan Asia stocks, ratings are based on a stock's total return relative to the average total return of the relevant country or regional benchmark; prior to 2nd October 2012 U.S. and Canadian ratings were based on (1) a stock's absolute total return potential to its current share price and (2) the relative attractiveness of a stock's total return potential within an analyst's coverage universe. For Australian and New Zealand stocks, 12-month rolling yield is incorporated in the absolute total return calculation and a 15% and a 7.5% threshold replace the 10-15% level in the Outperform and Underperform stock rating definitions, respectively. The 15% and 7.5% thresholds replace the +10-15% and -10-15% levels in the Neutral stock rating definition, respectively. Prior to 10th December 2012, Japanese ratings were based on a stock's total return relative to the average total return of the relevant country or regional benchmark.

**Restricted (R) :** In certain circumstances, Credit Suisse policy and/or applicable law and regulations preclude certain types of communications, including an investment recommendation, during the course of Credit Suisse's engagement in an investment banking transaction and in certain other circumstances.

**Volatility Indicator [V] :** A stock is defined as volatile if the stock price has moved up or down by 20% or more in a month in at least 8 of the past 24 months or the analyst expects significant volatility going forward.

Analysts' sector weightings are distinct from analysts' stock ratings and are based on the analyst's expectations for the fundamentals and/or valuation of the sector\* relative to the group's historic fundamentals and/or valuation:

**Overweight :** The analyst's expectation for the sector's fundamentals and/or valuation is favorable over the next 12 months.

**Market Weight :** The analyst's expectation for the sector's fundamentals and/or valuation is neutral over the next 12 months.

**Underweight :** The analyst's expectation for the sector's fundamentals and/or valuation is cautious over the next 12 months.

*\*An analyst's coverage sector consists of all companies covered by the analyst within the relevant sector. An analyst may cover multiple sectors.*

Credit Suisse's distribution of stock ratings (and banking clients) is:

#### Global Ratings Distribution

Rating	Versus universe (%)	Of which banking clients (%)
Outperform/Buy*	44%	(54% banking clients)
Neutral/Hold*	40%	(49% banking clients)
Underperform/Sell*	13%	(46% banking clients)
Restricted	3%	

*\*For purposes of the NYSE and NASD ratings distribution disclosure requirements, our stock ratings of Outperform, Neutral, and Underperform most closely correspond to Buy, Hold, and Sell, respectively; however, the meanings are not the same, as our stock ratings are determined on a relative basis. (Please refer to definitions above.) An investor's decision to buy or sell a security should be based on investment objectives, current holdings, and other individual factors.*

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#### Price Target: (12 months) for Alder Biopharmaceuticals (ALDR.OQ)

**Method:** Our rounded \$20 target includes \$15 for ALD-403, \$4 for Clazakizumab, and \$1.50 for its NOLs. Our \$20 valuation is justified by a fully-taxed, probability weighted, product level DCF for each of the two clinical stage programs plus the value of future NOLs. We assume an ex-US partner for ALD403 and significant dilution from future equity raises prior to profitability. For our DCF analysis, we use a 12% discount rate and 35% tax rate.

**Risk:** Risks to our \$20 TP include: 1) unexpected negative result for proprietary or partnered clinical program, 2) financing risk from expected future equity raises, 3) unexpected strong clinical result(s) from the competition in the migraine and RA settings, and 4) significant delay in one or more clinical programs that pushes potential approval timeline(s) out.

#### Price Target: (12 months) for Bristol Myers Squibb Co. (BMY.N)

**Method:** Our TP of \$59 for BMY is based on 75/25 blend of DCF value (\$60) and forward P/E (\$53). We apply 7% WACC and perpetuity growth forecast of 1.5% for DCF valuation and 30.0 times 2014 EPS of \$1.78 for P/E valuation.

**Risk:** Key risks to our target price of \$59 are two fold: (1) Pipeline failures, particularly in the immuno-oncology space could cause estimates to come down, and (2) underperformance of core franchises could bring longer-term estimates on these key franchises down.

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