

Equity Research

Healthcare | Biotechnology

ARIAD Pharmaceuticals, Inc.

Iclusig Comes Back With a New Label and REMS; Upgrade to

Outperform and Increase Price Target to \$12

On Friday, December 20, Ariad announced that it has reached agreement with the

FDA for immediate reauthorization of Iclusig marketing in the United States, with a

narrower label and accompanying Risk Mitigation Strategy (REMS) and postmarketing

requirements (PMRs). Ariad plans to resume shipping of Iclusig by mid-January 2014. The new label stipulates that Iclusig is indicated in adult patients with

T315I-positive chronic myeloid leukemia (CML) or T315I-positive Philadelphia chromosome positive acute lymphoblastic leukemia (Ph+ ALL), or in adult patients with

CML and Ph+ ALL where no other tyrosine kinase inhibitor (TKI) therapy is indicated. We

note that on October 31, the Food and Drug Administration (FDA) suspended marketing

of Iclusig based on the risk of life-threatening blood clots and severe narrowing of blood

vessels associated with Iclusig treatment. We had been expecting the recommercialization

of Iclusig with a narrower label, and we consider the REMS

accompanied by four PMRs without an Elements to Assure Safe Use (ETASU) to be a

favorable. We discuss the new label, REMS, and PMRs in detail herein.

We are upgrading Ariad shares to Outperform and increasing our price target from

\$3 to \$12 (exhibit 1, on page 5), based on the following: 1) limited downside with

REMS and PMRs in place, in our opinion; 2) positive physician feedback during ASH

and high number of single-agent INDs filed during marketing suspension; 3) potential for safer administration of Iclusig with lower doses in the

future; 4)

potential attempt at the frontline setting at lower doses as long-term upside; 5)

other potential indications of Iclusig that are not included in our model: GIST, and

NSCLC with FGFR and RET mutations; and 6) valuation: although the addressable patient population in 2014 is cut in half because of the narrower label

(from 2,500

to 1,300), the incidence is still substantial and the Iclusig patient population will

build over time. We have increased our peak worldwide Iclusig revenue forecast to \$747

million in 2026 from our previous estimate of \$275 million. Our revised probability-adjusted

NPV now assumes \$10 per share for Iclusig and \$2 for AP26113, compared with our previous estimate of \$1 and \$2 per share, respectively.

- Iclusig is now accompanied by a REMS and PMRs without a dedicated restricted distribution plan, thus enabling relatively easy growth with limited downside risk, in our opinion. We had expected an ETASU in the REMS that could impose greater restrictions in the distribution of Iclusig. We believe

with the new label, REMS, PMRs, and no ETASU, associated risks can be identified

and managed without severely impeding Iclusig uptake and sales growth. From a regulatory perspective, we believe that Iclusig has been de-risked in the near

term until perhaps 2016-2018 when we expect the readout of the required randomized control study (part of the PMRs) assessing the long-term safety of Iclusig treatment.

Ariad Pharmaceuticals is a biopharmaceutical company based in Cambridge, Massachusetts. The

company focuses its research, development, and commercial efforts on the oncology space, in

particular leukemia and lung cancer.

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Please consult pages 7-8 of this report for all disclosures. Analyst certification is on page 7.

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December 23, 2013

Stock Rating:

Symbol:

Price:

Outperform

Company Profile: Aggressive Growth

Price Target:

ARIA (NASDAQ)

Market Value (mil.):

Fiscal Year End:

\$6.43 (52-Wk.: \$2-\$23)

\$1,025

December

Long-Term EPS Growth Rate:

Dividend/Yield:

Estimates

EPS FY

CY
Sales (mil.)
Valuation
FY P/E
CY P/E
None
2012A 2013E 2014E
\$-1.34 \$-1.54 \$-0.78
\$-1.54 \$-0.78
109
1
44
NM NM NM
NM NM
Trading Data (FactSet)
Shares Outstanding (mil.)
Float (mil.)
Average Daily Volume
\$12.00
185
179
15,567,546
Financial Data (FactSet)
Long-Term Debt/Total Capital (MRQ) 0.2
Book Value Per Share (MRQ)
Enterprise Value (mil.)
EBITDA (TTM)
1.4
973.0
-256.8
Enterprise Value/EBITDA (TTM) -3.8x
Return on Equity (TTM)
-132.7
Two-Year Price Performance Chart
\$25
\$20
\$15
\$10
\$5
\$0
12/30/11
12/31/12
Sources: FactSet, William Blair & Company
estimates

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- Of the 640 patients on therapy at the end of October at the time of marketing suspension, 350 patients are on treatment under single-patient investigational INDs, including 260 who were on treatment before the suspension and 90 who were new patients. We note that since launch in the United States in January 2013, over 1,300 patients have been treated with Iclusig, with 640 on active treatment through the end of October. Management commented that since marketing suspension, 350 patients have continued treatment under single patient investigational new drug (IND) applications as required by the FDA, including 90 new patients over the 1.5-month period. Interestingly, those under the treatment INDs comprise second-line patients (about 20%) as well as third-line patients (about 30%), and later lines of therapy accounted for another 40%, with the remaining 10% being those with the T315I mutation. Given such a breakdown, we suspect that the relaunch will likely go well, assuming treatment IND patients come on line immediately, coupled with the high level of interest expressed by physicians at the recent ASH meeting.

- Key opinion leaders we spoke with at ASH are keeping patients on Iclusig but on lower maintenance doses, and are actively managing and monitoring patients. For patients who failed Gleevec and second-generation products such as Tasigna or Gleevec, as well as patients with the T315I mutation, Iclusig is the only option. Key opinion leaders advocated using Iclusig intelligently and selectively by excluding patients with high risk factors; aggressively managing high blood pressure, high lipids, and other cardiovascular symptoms; and using the lowest doses possible.

- Lower maintenance doses might improve safety. At ASH 2013, Cortez et al. (abstract No. 650) reported that factors significantly associated with arterial thrombotic adverse events included old age ($p < 0.0001$), history of diabetes ($p = 0.0003$), history of ischemic events ($p = 0.0087$), and higher dose intense to time of first event ($p = 0.0009$). Further, every 15 mg/day dose reduction resulted in predicted 40% reduction in risk of arterial thrombotic events. These data support re-evaluating Iclusig at lower doses.

- Although lower maintenance doses do not appear to compromise efficacy, it is unclear whether a lower induction dose would. Ariad will initiate a study in relapsed/refractory (R/R) patients in the second half of 2014 to evaluate Iclusig at a 30 mg starting dose, followed by the maintenance dose of 15 mg. We note that this study will be a post-marketing requirement (PMR), which will determine the true risk of vascular occlusions as well as the safety of the 45 mg starting dose. It is unclear whether the 30 mg dose would be as efficacious as the 45 mg dose to

induce as deep and durable a response. But such a strategy could decrease the risk of thrombotic events dramatically and is worth evaluating, in our opinion. Lastly, positive results from this study may serve as the impetus for use in the frontline at lower doses.

- Phase II Iclusig studies in other indications, GIST and FGFR/RET lung cancer, will reopen and patients reconsented once Iclusig returns to market; data in GIST could be presented at the 2014 ASCO. Management commented that Iclusig studies in these indications will continue and doses are likely to be reduced as well. As treatment duration is much shorter in solid tumor patients than in CML patients, there could be less risk or concerns in these indications.

We have updated our model to incorporate the revised Iclusig label in our estimates. We now estimate peak worldwide sales in 2026 at \$745 million compared with our previous estimate of \$275 million. As a result, we are increasing our price target from \$3 to \$12 based on the following assumptions:

- A peak market penetration in the second-line CML setting for Iclusig at 14% and 12% in the United States and Europe, respectively. As a result, we estimate peak sales from the second-line setting at \$90 million and \$25 million in the United States and Europe, respectively, in 2026.
- We estimate Iclusig's peak market penetration in the third-line CML setting at 80% and 75% in the United States and Europe, respectively. As a result, we estimate peak sales from the third-line setting at \$278 million and \$112 million in the United States and Europe, respectively, in 2026.
- We estimate Iclusig's peak penetration into the T315I patient population at 90% for both regions. We estimate peak sales in 2026 from patients with T315I mutation at \$102 million and \$69 million for the United States and Europe, respectively.

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- We estimate the number of total patients treated at peak in 2026 at 7,200, with over 3,200 patients treated in the United States and about 4,000 patients treated in Europe. We also estimate the number of second-line, thirdline, and T315I patients treated at peak in the United States in 2026 are 625, 1,920, and 705, respectively. For Europe, we estimate the number of second-line, third-line, and T315I patients treated at peak are 507, 2,150, and 1,330, respectively.
- We maintain our pricing assumptions, yearly price increases, and gross-to-net discounts for Iclusig both in the United States and Europe. For the U.S. market, we continue to assume a gross list price for Iclusig of \$124,000 for 2014, with 4% annual price increases and a gross-to-net discount of 9%. In Europe, we continue to assume an average gross price of \$75,000 across the continent, flat pricing, and a gross-to-net discount of 13%.
- Our worldwide peak sales estimates for Iclusig in 2026 increased from \$275 million to \$745 million, with \$470 million in sales attributed to the United States, \$210 million attributed to Europe, and \$67 million attributed to additional territories. Our previous estimate for peak sales of \$275 million included estimates of \$199 million, \$64 million, and \$16 million for the United States, Europe, and additional territories, respectively.
- We increased our total Iclusig sales for 2014 and 2015 to \$108.8 million and \$212.8 million, respectively, compared with our previous estimates of \$69.7 million and \$84.2 million, and consensus of \$70.8 million and \$169.5 million. We now estimate U.S. Iclusig revenues for 2014 and 2015 at \$65.6 million and \$158.3 million, respectively, versus our previous estimate of \$32.2 million and \$40.7 million. In addition, we increased our estimates of Iclusig revenue from Europe for 2014 and 2015 to \$42.9 million and \$54.3 million, respectively, compared with our previous estimates of \$37.4 million and \$43.5 million. On the bottom line, we now estimate a net loss per share for 2014 and 2015 of \$0.78 and \$0.11, respectively, compared with our previous per share loss estimate of \$0.98 and \$0.76 and consensus of \$0.96 and \$0.60.
- As a result, we have increased our 12-month price target to \$12 from \$3 (exhibit 1). Our current valuation is based on our probability-adjusted net present value (NPV) model and assumes Iclusig in CML constitutes the majority of Ariad's valuation at \$10 per share, compared with our previous estimate of \$1. We continue to estimate AP26113 is valued at \$2 per share, with peak sales of \$280 million and 81% probability in ALK+ NSCLC. Based on such assumptions, our probability-adjusted NPV model now derives a 12-month fair value for Ariad at \$12 per share.

Iclusig is now indicated for those with the T315I mutation and in salvage therapy, albeit with a caveat. The new label allows Iclusig to be used as a third-line agent after Gleevec and a second-generation TKI such as Tassigna and Sprycel. However, as 60% of patients in the United States and 50% in Europe are initiating therapy with Tassigna or Sprycel, Iclusig could still potentially be used as second-line therapy in these patients after they fail. Although the company noted it can only market Iclusig as second line to those with the T315I mutation, second-line patients under the treatment IND account for 20% of the total INDs. Given the treatment paradigm, we are therefore optimistic about Iclusig's opportunity. Below, we provide further details on the revised label.

- Iclusig is now indicated for the following: 1) adult patients with T315I-positive chronic myeloid leukemia (CML, chronic phase, accelerated phase, or blast phase) or T315I-positive Philadelphia chromosome positive acute lymphoblastic leukemia (Ph+ ALL) and 2) adult patients with chronic phase, accelerated phase, or blast phase CML or Ph+ ALL for whom no other tyrosine kinase inhibitor (TKI) therapy is indicated.

- The revised "Warnings and Precautions" section includes new language detailing the risk of vascular occlusion events. Of note, the new label describes the risk of arterial and venous thrombosis and occlusions events as occurring in at least 27% of treated patients.

- The 45 mg starting dose remains part of the revised label, but the "Dosing and Administration" section of the label has been revised to state that the optimal Iclusig dose has not been identified.

The revised Iclusig label will be accompanied by a REMS and associated PMRs. The REMS consists of a Medication Guide and a communication plan to be accompanied by four post-marketing requirements (PMRs) to better understand the risk of occlusions while increasing patient and prescriber awareness.

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- The REMS program will consist of a communication plan to better educate patients and prescribers about the increased risk of occlusions and the revised indication. This will consist of letters to be mailed out to prescribing healthcare professionals informing them of the associated risks and a fact sheet and summary page also informing healthcare professionals about the risk to be distributed at meetings and disseminated through various medical journals. We note that the level of awareness will be evaluated by the FDA during its REMS assessment, which will be documented in the expected approval letter.
- There will be a number of PMRs, which, in our opinion, will better assess the true risk associated with Iclusig. Ariad will be held to four PMRs: 1) a pharmacovigilance assessment of risk factors associated with vascular occlusive events and an assessment of patient management and consequences with those who experience vascular occlusive events; 2) a prospective observation assessing the incidence of vascular occlusive events associated with Iclusig with or without anticoagulant or antiplatelet agents; 3) a follow-up of patients who were previously enrolled in the Phase I, II, and III (EPIC) studies to better understand the long-term safety of Iclusig; and 4) In the second half of 2014, a trial will be initiated to assess the long-term safety of Iclusig treatment, including the long-term risk of vascular occlusive events over time.

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Exhibit 1

ARIAD Pharmaceuticals, Inc.

Sum-of-Parts Fair Value

(dollars in thousands)

Drug

Iclusig—CML

Worldwide

AP26113—ALK+ NSCLC

Worldwide

Subtotal

Net Cash at Year-end 2014

Net Present Value of additional Gain (Loss)*

Sum-of-Parts Fair Value

* Includes costs not directly related to programs above

Sources: Company reports and William Blair & Company, L.L.C. estimates

2678.220028

Peak Sales

Stage of

Development

\$746,822 Marketed

\$280,018 Phase I/II

Estimated

Launch Date

January 2013/

July 2013

H2:2016

Probability of

Commercialization

100%

81%

Percentage of

Sales to Company

100%

100%

ProbabilityAdjusted

NPV

\$1,843,975

\$325,268

\$2,169,243

\$63,406

(\$22,727)

\$2,209,922

Value

per Share

\$9.85

\$1.74

\$11.59

\$0.34

(\$0.12)

\$11.81

Percentage of
Fair Value

83.4%

14.7%

98.2%

2.9%

(1.0%)

100.0%

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 Exhibit 2
 ARIAD Pharmaceuticals, Inc.
 Income Statement
 (dollars in millions)
 2011
 FY:11A
 Revenues
 Iclusig - U.S. revenue
 Iclusig - EU revenue
 AP26113 - U.S. revenue
 AP26113 - EU revenue
 Royalties
 License and collaboration revenue
 Service revenue
 Total Revenues
 Expenses
 COGS
 R&D expense
 SG&A expense
 Total Operating Expenses
 Operating income
 Interest income/(expense)
 Revaluation of warrant liability
 Pretax income/(loss)
 Provision for income taxes/(income)
 Net Income/(Loss)
 GAAP EPS, basic
 Weighted average shares outstanding, basic
 \$0
 -
 -
 -
 -
 25,189
 111
 25,300
 -
 77,743
 24,380
 102,123
 (76,823)
 (65)
 (46,715)
 (123,603)
 -
 2012
 FY:12A
 \$0
 -
 -

-
-
490
68
558
-
144,710
60,909
205,619
(205,061)
113
(15,924)
(220,872)
-
(\$123,603) (\$220,872)
(\$0.93)
132,375
Sources: Company reports and William Blair & Company, L.L.C. estimates
164,955
(\$1.34)
Q1A
\$6,400
-
-
-
-
64
-
6,464
269
41,263
29,481
71,013
(64,549)
(62)
-
(64,611)
59
(\$64,670)
(\$0.36)
178,541
Q2A
\$13,934
-
-
-
-
77
-
14,011
228

40,668
42,101
82,997
(68,986)
87
-
(68,899)
86
(\$68,985)
(\$0.37)
184,726
2013
Q3A
\$16,658
-
-
-
-
74
-
16,732
415
45,145
37,395
82,955
(66,223)
(6)
-
(66,229)
110
(\$66,339)
(\$0.36)
185,238
Q4E
\$5,380
1,329
-
-
-
64
-
6,773
335
47,402
40,761
88,498
(81,726)
(6)
-
(81,732)
113

FY:13E

\$42,372

1,329

-

-

-

279

-

43,980

1,247

174,478

149,738

325,463

(281,484)

13

-

(281,471)

368

(\$1.54)

2014

FY:14E

\$65,689

42,854

-

-

-

250

-

108,793

5,195

140,685

106,159

252,040

(143,247)

(24)

-

(143,271)

1,197

(\$81,844) (\$281,838) (\$144,468)

(\$0.44)

185,338

183,461

185,588

(\$0.78)

2015

FY:15E

\$158,277

54,345

-

-

-

173
-
212,796
10,303
133,337
87,787
231,427
(18,632)
(24)
-
(18,656)
2,174
(\$20,829)
(\$0.11)
188,773
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appropriate by the analyst.

DOW JONES: 16,221.14

S&P 500: 1,818.32

NASDAQ: 4,104.74

ARIAD Pharmaceuticals, Inc. (ARIA)

Dec 20, 2010 - Dec 20, 2013

\$10

\$15

\$20

\$25

\$0

\$5

12/31/10

Source: FactSet and William Blair

12/30/11

12/31/12

Legend: I = Initiation, RI = Reinitiated, @ = Analyst Change PT = Price Target

Previous Close: \$6.43

9/30/13 - PT:\$26

10/9/13 - PT:\$7

10/18/13 - M - PT:\$3

7/30/12 - I-0 - PT:\$25

10/22/12 - PT:\$28

Current Rating Distribution (as of 11/30/13)

Coverage Universe

Percent

Outperform (Buy)

Market Perform (Hold)

Underperform (Sell)

61

35

1

Inv. Banking Relationships*

Outperform (Buy)

Percent

Market Perform (Hold)

Underperform (Sell)

11

1

0

*Percentage of companies in each rating category that are investment banking clients, defined as companies for which William Blair has received compensation for investment banking services within the past 12 months.

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Outperform (O) – stock expected to outperform the broader market over the next 12 months; Market Perform (M) – stock expected to perform

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