

Equity Research

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Agile Therapeutics, Inc. (AGRX-\$6.78)

Rating: BUY

Target Price: \$17.00

Reinventing the Contraceptive Patch: Initiating Coverage with a BUY Rating and \$17 PT

<u>REV</u>	<u>1Q</u>	<u>2Q</u>	<u>3Q</u>	<u>4Q</u>
2013A	—	—	—	—
2014E	0.0A	0.0E	0.0E	0.0E
2015E	—	—	—	—
<u>EPS</u>	<u>1Q</u>	<u>2Q</u>	<u>3Q</u>	<u>4Q</u>
2013A	—	—	—	—
2014E	0.09A	(0.53)E	(0.51)E	(0.64)E
2015E	—	—	—	—
<u>FY</u>	<u>2013A</u>	<u>2014E</u>	<u>2015E</u>	
REV	0.0A	0.0E	0.0E	
EPS	(0.29)A	(1.70)E	(1.51)E	

- **We initiate coverage of Agile Therapeutics with a BUY rating and \$17 PT:** Agile is developing Twirla, a Phase III, low-dose estrogen contraceptive patch that we believe has the potential to approximate the Ortho Evra launch trajectory. We expect positive data from the Phase III trial in mid-2015, followed by product launch in early 2017. Even under conservative risk-adjusted assumptions we believe that Twirla can attain over \$300M in peak sales, and we think that this opportunity makes Agile an attractive, late-stage take-out target to a larger company focused on women's health. We see the stock as undervalued following the caution and recent sell-off in the biotech sector and initiate coverage with a BUY rating and \$17 PT.
- **Simple story, with a lot to like:** Twirla will compete in a large and lucrative contraceptive market that has been growing since the passage of the Affordable Care Act. We believe that a contraceptive patch would generate significant patient and physician demand given that J&J's Ortho Evra quickly attained 10% market share before safety concerns about its estrogen exposure led to the brand's decline. Twirla has demonstrated lower estrogen exposure and estrogen-associated adverse events than Ortho Evra, so we think that doctors would easily understand the safety benefits of the product, which should facilitate its launch. We like category pricing in contraceptives since a recently launched generic version of Ortho Evra is priced at a premium to branded oral contraceptives. We believe that management is highly experienced and has realistic expectations. Finally, there has been significant M&A activity in women's health, which should also benefit Agile, in our view.
- **The Twirla Phase III trial and NDA have been de-risked via a prior failure:** Agile has received extensive FDA guidance with respect to study design, trial endpoints, and patient inclusion/exclusion criteria after receiving a complete response letter in early 2013. We think management has learned from its prior mistakes and strengthened its ranks with more experienced personnel. The company should be able to assure stronger results in this next trial via careful selection of more appropriate clinical sites and contraceptive-using patients, in our view. Finally, FDA has also completed its pre-approval inspection of Twirla's manufacturing facility, which minimizes another risk to approval.
- **Valuation and risks:** We value Agile via DCF (13% WACC and 1% terminal growth rate) to account for the clinical risk associated with the Phase III Twirla trial. Key risks to the story include the aforementioned clinical risk (we also risk-adjust our revenue estimates by 60%), financing risk in mid-2015, and slower-than-expected commercial launch of Twirla.

Current Statistics

Market Cap (\$Mil)	\$126.1	Float Shares (Mil):	18.600
Avg. Daily Trading Volume (3 mo.):	NA		
Shares Out (Mil):	18.592		

The Disclosure Section may be found on pages 27 - 30.

*We initiate coverage of
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price target*

Summary

- **We initiate coverage of Agile Therapeutics with a BUY rating and \$17 PT:** Agile is developing Twirla, a Phase III, low-dose estrogen contraceptive patch that we believe has the potential to approximate the Ortho Evra launch trajectory. We expect positive data from the Phase III trial in mid-2015, followed by product launch in early 2017. Even under conservative risk-adjusted assumptions we believe that Twirla can attain over \$300M in peak sales (which represents less than half the market share attained by Ortho Evra), and we think that this opportunity makes Agile an attractive, late-stage take-out target to a larger company focused on women's health. We see the stock as undervalued following the caution and recent sell-off in the biotech sector and initiate coverage with a BUY rating and \$17 PT.
- **Simple story, with a lot to like:** Twirla will compete in a large and lucrative contraceptive market that has been growing since the passage of the Affordable Care Act. We believe that a contraceptive patch would generate significant patient and physician demand given that J&J's Ortho Evra quickly attained 10% market share before safety concerns about its estrogen exposure led to the brand's decline. Twirla has demonstrated lower estrogen exposure and estrogen-associated adverse events than Ortho Evra, so we think that doctors would easily understand the safety benefits of the product, which should facilitate its launch. We like category pricing in contraceptives since a recently launched generic version of Ortho Evra is priced at a premium to branded oral contraceptives. We think the prescriber universe can be easily targeted with a small specialty sales force, which keeps SG&A costs low. We believe that management is highly experienced and has realistic expectations. Finally, there has been significant M&A activity in women's health, which should also benefit Agile, in our view.
- **The Twirla Phase III trial and NDA have been de-risked via a prior failure:** Agile has received extensive FDA guidance with respect to study design, trial endpoints, and patient inclusion/exclusion criteria after receiving a complete response letter in early 2013. We think management has learned from its prior mistakes and strengthened its ranks with more experienced personnel. The company should be able to assure stronger results in this next trial via careful selection of more appropriate clinical sites and contraceptive-using patients, in our view. Finally, FDA has also completed its pre-approval inspection of Twirla's manufacturing facility, which minimizes another risk to approval.
- **Valuation and risks:** We value Agile via discounted cash flow analysis (13% WACC and 1% terminal growth rate) to account for the clinical risk associated with the Phase III Twirla trial, which generates our \$17 PT. We use similar valuation metrics in other clinical-stage companies in our universe such as Evoke Pharma and Eagle Pharmaceuticals. Key risks to the story include the aforementioned clinical risk (we also risk-adjust our revenue estimates by 60%), financing risk in mid-2015, and slower-than-expected commercial launch of Twirla. We don't view Mylan's generic version of Ortho Evra to be a direct competitor to Twirla since the products are not bioequivalent or substitutable.

Company History

Agile Therapeutics is a development-stage specialty pharmaceutical company with a focus in the transdermal hormonal contraceptive space. Agile was incorporated in 1997 and has focused its efforts on Twirla, its lead product candidate, which is expected to enter a Phase III clinical trial in 3Q:14. Exhibit 1 displays recent financing activity for the company, which held its initial public offering on May 22, 2014, along with a 1.4-for-one stock split effective May 7.

Exhibit 1: Agile Therapeutics Financing

Date	Event	Funds Raised (\$ in millions)
May 2010	Series B Stock Purchase Agreement	\$23.3
June 2010 - March 2012	Series B Stock Purchase Agreement	\$21.8
May 2012	Convertible Note Purchase Agreement	\$6.0
July 2012	Series C Preferred Stock Purchase Agreement	\$16.9
December 2012	Oxford Term Loan and Security Agreement	\$15.0
May 2014	Initial Public Offering	\$51.2

Source: Company reports and Cantor Fitzgerald research

Additionally, the company has debt that was issued in December 2012 at a fixed annual interest rate of 9.2%, and it recently extended the interest-only period through February 2015. This loan matures on July 1, 2017, and management plans to pay down approximately \$5 million of principal per year.

Management indicated that it hopes to use approximately \$31 million of the IPO proceeds to fund the Twirla Phase III program, with the remainder helping fund equipment validation and manufacturing capacity expansion, as well as work on its extended regimen line extension. Management expects to have sufficient cash through the release of its Phase III Twirla data in 2H:15.

Industry Overview

Exhibit 2 summarizes the entrenched companies in the contraceptive space as well as a sampling of development stage specialty pharmaceutical companies who held recent initial public offerings.

Exhibit 2: Companies Active in Contraceptive Products and Development Stage Specialty Pharmaceutical Companies

Women's Health Companies	Ticker	Price as of 6/16/14	Market Cap (mil)	EPS 2014E	EBITDA 2014E	P/E 2014E	EV/ EBITDA	EV (mil)
Actavis Plc	ACT	\$210.38	\$36,700	\$13.56	4,550	15.51	9.93	\$45,180
Bayer AG	BAYN-DE	\$139.57	\$115,419	\$8.29	12,225	16.84	10.53	\$128,787
Johnson & Johnson	JNJ	\$102.45	\$289,841	\$5.88	24,892	17.42	11.35	\$282,413
Merck & Co., Inc.	MRK	\$58.07	\$169,702	\$3.48	16,056	16.67	11.38	\$182,750
Teva Pharmaceutical Industries	TEVA	\$51.70	\$44,042	\$4.72	6,109	10.96	9.00	\$54,954
Average		\$112.43	\$131,141	\$7.19	12,767	15.48	10.44	\$138,817
Development Stage IPO Companies								
AcelRx Pharmaceuticals, Inc.	ACRX	\$10.35	\$448	(\$1.06)	(35)	(9.75)	(10.41)	\$369
Eagle Pharmaceuticals, Inc.	EGRX	\$12.22	\$171	(\$1.35)	(18)	(9.07)	(3.00)	\$53
Evoke Pharma, Inc.	EVOK	\$8.00	\$49	(\$2.67)	(16)	(2.99)	(1.76)	\$29
Flexion Therapeutics, Inc.	FLXN	\$13.03	\$204	(\$2.82)	(45)	(4.62)	(0.58)	\$26
Heron Therapeutics Inc	HRTX	\$11.32	\$271	(\$3.30)	NA	(3.43)	NA	\$212
Ocera Therapeutics, Inc.	OCRX	\$7.23	\$112	(\$1.81)	(35)	(4.01)	(1.95)	\$68
Recro Pharma, Inc.	REPH	\$7.24	\$56	(\$2.73)	NA	(2.65)	NA	(\$17)
Revance Therapeutics, Inc.	RVNC	\$29.64	\$559	(\$3.28)	NA	(9.04)	NA	\$256
Synergy Pharmaceuticals, Inc.	SGYP	\$4.14	\$388	(\$0.88)	(80)	(4.70)	(3.90)	\$310
Average		\$11.46	\$250.90	(\$2.21)	(38)	(5.59)	(3.60)	\$145

Source: Company reports and Cantor Fitzgerald research

We Note That There is Significant M&A Activity in Women's Health

Warner Chilcott, which was acquired in 2013 by Actavis PLC, had an established women's health franchise encompassing oral contraception and hormone replacement products. Its acquisition price of approximately \$8.5 billion represented a 34 percent premium to Warner Chilcott's 30-day volume-weighted average closing price at the time of deal disclosure, providing Actavis with tax synergies and enhancing the company's existing presence in the oral contraceptive business. (Loestrin 24 and LoLoestrin totaled over \$550 million in sales in 2013.) Johnson & Johnson developed and

commercialized Ortho Evra, the only branded FDA-approved contraceptive patch on the market. Bayer commercialized the Yaz franchise of oral contraceptives as well as its Mirena intrauterine device. Merck & Co. is also a competitor in this space, most notably with the NuvaRing, which currently holds approximately 6% of the market and was the top selling combined hormonal contraceptive (CHC) product in 2013, also totaling over \$550 million in sales¹.

There are also a number of developmental-stage companies in women's health, including fertility companies such as OvaScience, Inc. and Nora Therapeutics, which are developing products to increase the success of IVF treatments and improve the likelihood of birth. Additionally, there are female sexual health-focused companies such as Apricus Biosciences, Sprout Pharmaceuticals, Inc. and S1 Biopharma, Inc., which are attempting to address the treatment of sexual dysfunction and arousal disorders.

Contraceptive Market Background

We note that nearly half of the pregnancies that occur in the U.S. each year are unplanned. The U.S. was the first country to approve a hormonal contraceptive, with the approval of the first contraceptive pill in 1960. The latest data from the Centers for Disease Control (CDC), from 2006–2010, indicate that approximately 25% of women aged 15–44 use some form of hormonal contraception, which amounts to approximately 15.4 million women in the United States.

Components of CHCs are well known

Hormonal contraceptives come in several forms—oral pill, patch, vaginal ring, intrauterine device (IUD), injection—and are composed of synthetic estrogens and/or progestins. These forms are summarized in Exhibit 3. There are three synthetic FDA-approved estrogens for use in contraceptive products: ethinylestradiol (EE), mestranol, and estradiol valerate. EE is the synthetic estrogen used in nearly all CHCs today.² There are 10 different progestins that have been used in contraceptives sold in the United States, two popular examples of which are norelgestromin and levonorgestrel (LNG). The progestin component provides most of the contraceptive effect, while the estrogen component primarily provides cycle control. The progestin exerts its contraceptive effect by inhibiting ovulation and thickening cervical mucus. This thickening of the cervical mucus helps to prevent sperm from entering the upper genital tract. The estrogen component also decreases the maturation of the egg in the ovary.³

Newer progestins are accompanied by increased safety risks

The progestins used in CHC's are categorized by generations, based on their history of introduction in the United States. The first- and second-generation progestins, such as ethynodiol diacetate, LNG, and norethisterone, have been available in contraceptive formulations in the United States for over 25 years and are considered extremely safe. The third- and fourth-generation progestins, such as gestodene, drospirenone (DRSP) and etonogestrel, found in Yasmine/YAZ, NuvaRing and Nexplanon, were introduced more recently. Epidemiologic data suggest that CHCs containing third- and fourth-generation progestins (which represent approximately 34% of total CHC prescriptions) are associated with an increased risk of venous thromboembolism (VTE), as compared to those containing first- or second-generation progestins. For example, drospirenone-containing Yasmin/YAZ was the subject of a 2011 FDA Drug Safety and Risk Management Advisory Committee meeting due to concerns about adverse side effects. An FDA study found that DRSP increased the risk of VTE by 70-80% compared

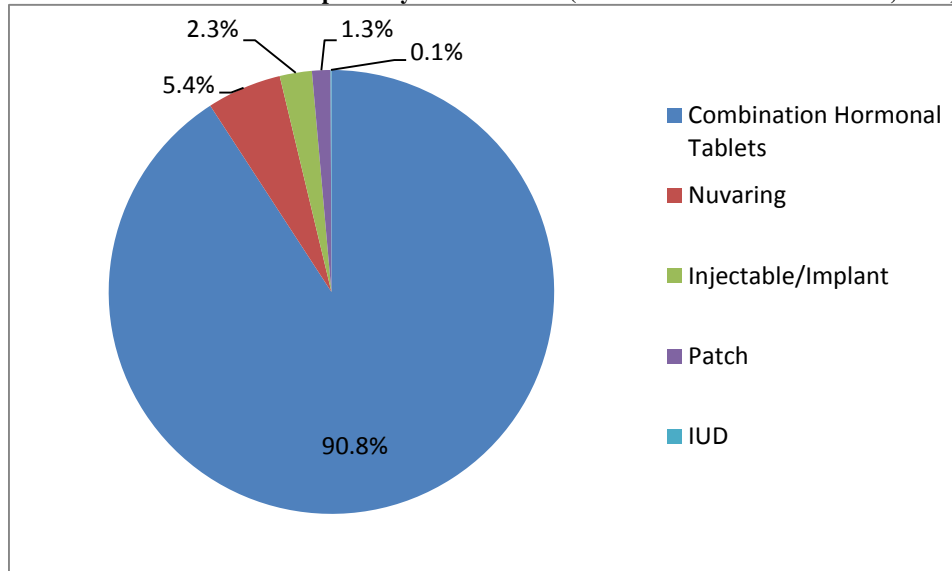
¹ <http://www.sec.gov/Archives/edgar/data/1261249/000104746914004768/a2220115zs-1a.htm> (pg 125)

² <http://www.sec.gov/Archives/edgar/data/1261249/000104746914004768/a2220115zs-1a.htm> (pg 101)

³ <http://www.sec.gov/Archives/edgar/data/1261249/000104746914004768/a2220115zs-1a.htm> (pg 101)

to lower-dose estrogen pills⁴—these results are also consistent with four other epidemiological studies reviewed by the agency. An additional warning referencing increased risk of thromboembolic events in combination with oral contraceptives containing DRSP is included in the labels for these medications, but is not Black-Boxed. The reason that products such as YAZ are able to remain commercially viable, in our view, is that they have a lower contraceptive failure rate (approximately 2% versus other birth control pills, which are closer to 3.5%)⁵, and are appealing in secondary indications such as acne and premenstrual dysphoric disorder.

Exhibit 3: Hormonal Contraceptives by Market Share (12 months ended December 31, 2013)



Source: Company reports, Symphony Health Solutions, and Cantor Fitzgerald research

Side effects are rare but serious

Hormonal contraceptives are generally well-tolerated and are safer than pregnancy. Two risks associated with hormonal contraceptives that are rare but serious adverse events are venous thromboembolisms (VTE) and arterial thrombotic events (ATE), which involve the formation of a blood clot in a vein or artery. These events can be life-threatening and typically present as either deep vein thrombosis (DVT) or pulmonary embolism (PE). Evidence supports that the increased risk of VTE in CHC users is dependent upon the estrogen dose (and exposure) and duration of use. Estrogen increases the formation of clotting factors in the liver and decreases production of elements that promote breakdown of blood clots. Most experts believe that progestins on their own have minimal to no impact on the clotting system, but some progestins, when combined with estrogen, can increase estrogen's effect on the clotting system. The likelihood of a woman spontaneously developing a VTE is very low, and the use of combination oral contraceptives increases the incidence only slightly and is much lower than in pregnancy. The incidence of VTE in a non-pregnant woman who does not use an oral CHC ranges from 1 to 5 cases per 10,000 woman-years (one woman-year is equivalent to one woman using a contraceptive for 12 months, or 13 cycles).⁶ Among oral CHC users, the incidence ranges from 3 to 12 cases per 10,000 woman-years. However, in pregnancy the incidence of VTE

⁴<http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/ReproductiveHealthDrugsAdvisoryCommittee/UCM288721.pdf> (pg 218)

⁵

<http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/ReproductiveHealthDrugsAdvisoryCommittee/UCM288721.pdf> (pg 178-180)

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<http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/ReproductiveHealthDrugsAdvisoryCommittee/UCM288721.pdf> (pg 181)

increases to 5 to 20 cases per 10,000 woman-years, and in the 12 weeks following delivery the incidence ranges from 40 to 65 cases per 10,000 woman-years.⁷

The Affordable Care Act is expected to be favorable to Agile

The Affordable Care Act (ACA), which went into effect in August 2012, requires that all insurance plans cover certain preventive services for women with no deductible, no co-insurance, and no co-payments required by the patient. This includes both contraceptive counseling and at least one covered product for each FDA-approved contraceptive method. Since the ACA went into effect, quarterly prescription data tracking volume growth for the CHC market has risen from negative growth to Y/Y positive growth between 4–5% in each quarter.⁸

The ACA has been a contentious topic both politically and economically, and many who disagree with its mandates have taken their case to the courts. A recent example of this is Hobby Lobby, a privately held craft-focused big-box retailer, which is suing the U.S. government with claims that providing health insurance to its employees violates the company's owners' religious beliefs by forcing them to cover the cost of certain contraceptives. How the Supreme Court rules in this case and others akin to it could have a major impact on reimbursement and thus an impact on overall contraceptive market growth. As it stands today, there remains some ambiguity in the ACA guidelines, and as a result there is variability in how insurance providers are interpreting, and therefore implementing, these changes in policy. Once current litigation surrounding the contraceptive portion of the ACA is resolved, we will have more color on what exactly is required of both employers and insurance companies, and will then be able to better forecast market potential and growth.

The prescriber base is easily targeted

Obstetricians and gynecologists (ObGyns) contribute nearly 50% of the U.S. contraception prescription volume, while Nurse Practitioners and Physician Assistants (often affiliated with an ObGyn practice) contribute an additional 23% of the prescriptions.⁹ The remaining prescriptions originate from General Practitioners. We note that there are over 700 Planned Parenthood health centers and nearly 4,500 school health clinics that regularly prescribe contraception as well. However, data from these facilities are not included in the IMS Health database, and therefore a notable amount of contraceptive prescription volume exists outside of many market share estimates and projections.

In 2013, despite widespread generic contraceptive availability, branded CHC products maintained a significant share of the market with 55% of dollar sales and 27% of total prescriptions.¹⁰ Sampling of products in the clinical setting is critical in the contraceptive space and is a key factor in why branded products continue to persist.

Ortho Evra's meteoric launch and market persistence suggest that there is high consumer demand for contraceptive patches

CHCs have been a staple among oral contraceptive agents for many years, but there is only one FDA-approved patch, Johnson & Johnson's Ortho Evra patch. Evra was introduced to the market in early 2002 and experienced rapid growth in popularity, achieving a greater than 10% share of the CHC market by late 2003. It was a great solution for users who are non-compliant with daily oral

⁷ <http://www.sec.gov/Archives/edgar/data/1261249/000104746914004768/a2220115zs-1a.htm> (pg. 101)

⁸ <http://www.sec.gov/Archives/edgar/data/1261249/000104746914004768/a2220115zs-1a.htm> (pg. 104)

⁹ <http://www.sec.gov/Archives/edgar/data/1261249/000104746914004768/a2220115zs-1a.htm> (pg. 3-4)

¹⁰ <http://www.sec.gov/Archives/edgar/data/1261249/000104746914004768/a2220115zs-1a.htm> (pg. 105)

contraceptive methods. However, despite its initial uptake, this growth was short-lived as users of Ortho Evra began to report thromboembolic events, forcing J&J to revise the drug label to include information that EE exposure with Evra is 60% higher than that of an oral CHC containing EE of 35 micrograms (the industry standard). This information was ultimately included in a Black Box warning, whereby Ortho Evra market share fell to 4% by the end of 2006 and 1.4% by the end of 2013.¹¹ Despite this rapid decline, Evra remained a \$150 million (2013 sales) product with no sales promotion, sampling, or marketing behind it.

Safety concerns ultimately curbed Evra use

A Citizen Petition was filed by Public Citizen Health Research in 2008 in an effort to withdraw approval of the Ortho Evra new drug application (NDA), which subsequently would remove the drug from the market. FDA denied the petition in August 2012. The petition used area under the time-concentration curve (AUC) methodology for comparing EE levels found in Evra with those in combined oral contraceptives COCs.¹² The agency's Advisory Committee, which met in December 2011, acknowledged in its response that based on AUC analysis overall EE exposure is substantially higher in Evra users compared to women using a COC containing 35 micrograms of EE. However, FDA argued that the clinical impact of such exposure is uncertain because peak concentrations of EE (C_{max}) are approximately 25% lower in Evra users. It remains unknown how EE AUC and EE C_{max} affect estrogen-related adverse events. Furthermore, studies which have directly compared the two methods use a linear approach in calculating an equivalent EE COC dose for Evra, but the FDA maintained that there are no adequate data available for COCs above 35 micrograms of EE, and a linear relationship between EE levels and adverse events could not be confirmed. The FDA also notes that data exist to indicate that EE AUC may not increase proportionally with dose.¹³ The Advisory Committee concluded that, "In the general population of women who desire contraception, the benefits of Ortho Evra for the prevention of pregnancy outweigh the risks,"¹⁴ and therefore the agency denied the Citizen Petition four years after it was filed. Instead, FDA recommended more prominent warning language in the label for the drug. Exhibit 4 highlights historical label changes over Evra's lifecycle to-date.

¹¹ <http://www.sec.gov/Archives/edgar/data/1261249/000104746914004768/a2220115zs-1a.htm> (pg 106)

¹² Citizens Petition (pg 1) (<http://www.regulations.gov/#!documentDetail;D=FDA-2008-P-0296-0023>)

¹³ Citizens Petition (pg 13)

¹⁴ Citizens Petition (pg 23)

Exhibit 4: Ortho Evra Label Changes

Date	Drug Label Changes
May-05	Revised original label to state that exposure to EE is greater than with a 20 microgram EE COC.
Nov-05	Added a bold text warning that AUC for EE was 60% greater than that for a 35 microgram EE COC, while Cmax was 25% lower.
Sep-06	Described possible increased risk of VTE in comparison to COC users.
Jan-08	Further described possible increased risk of VTE in comparison to COC users.
Oct-08	Further described possible increased risk of VTE in comparison to COC users.
Sep-09	Provided revised data relating to a possible increased risk of VTE in comparison to COC users.
Apr-10	Added new data regarding possible increased risk of VTE in comparison to COC users.
Mar-11	Added warning to make existing information about risk of VTE more prominent to healthcare providers

Source: FDA Briefing Document, December 9, 2011¹⁵; Company reports and Cantor Fitzgerald research
Cmax=maximum concentration; AUC=area under the curve; EE=ethinyl estradiol; COC=combined oral contraceptive;
VTE=venous thromboembolism

The recent launch of Mylan's Ortho Evra generic is not expected to grow the market or obstruct the launch of Twirla:

On April 16, 2014 Mylan announced the availability and launch of XULANE, its generic version of Ortho Evra (following an ANDA filing in 2007). We expect this generic to cannibalize sales of Johnson & Johnson's \$150 million product but do not anticipate any additional market expansion since the generic is unlikely to be promoted or sampled to physicians. Furthermore, this generic may still be saddled with the same physician safety concerns regarding VTE risk. XULANE is packaged as a single cycle box, with no replacement patches available in case one of the patches falls off or needs to be replaced. XULANE had captured 75% of Ortho Evra prescriptions as of the week ended June 6, 2014. The patch market grew +2.2% Y/Y in the last 12 months ended April 2014, which appears to be unrelated to the Xulane launch.

Company Overview

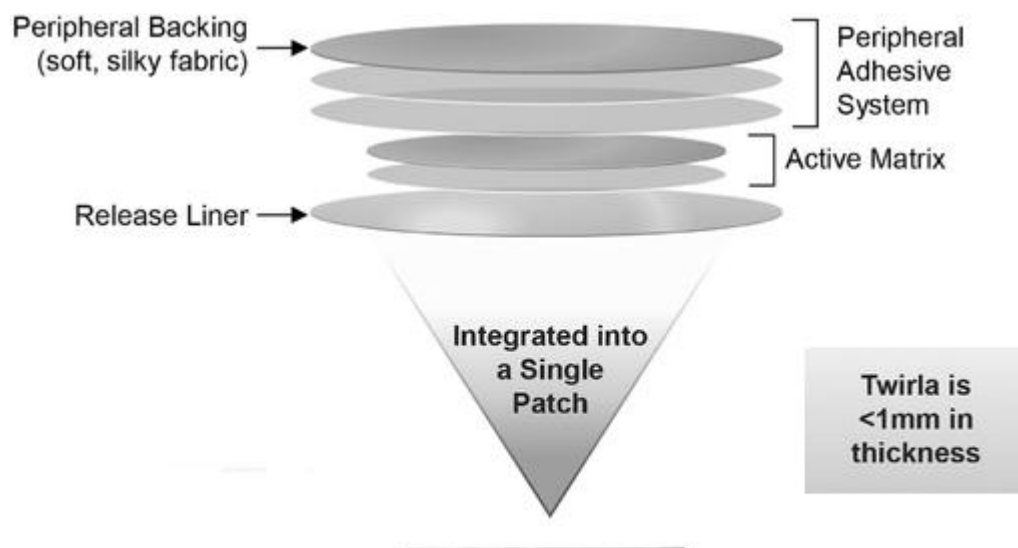
Agile Therapeutics is a specialty pharmaceutical company focused on the development and commercialization of new contraceptive products, with a primary focus on its transdermal patch technology, called Skinfusion. The company believes this technology to be superior to other currently available contraceptive patches, as it is intended to optimize patch adherence, stability, and patient acceptance. The company's flagship product candidate is Twirla, a once-weekly prescription contraceptive patch currently in Phase III clinical development. The company is targeting the estimated \$5.6 billion U.S. hormonal contraceptive market.

¹⁵ Background document for joint meeting of the Advisory Committee for Reproductive Health Drugs and the Drug Safety and Risk Management Advisory Committee. NDA 21-180, Ortho Evra. December 9, 2011.

Twirla is a comfortable patch comprised of a low-dose estrogen and a safe, well-known progestin

Agile's flagship product, Twirla, has been in development for over a decade. It is a combination hormonal transdermal patch that delivers approximately 30 micrograms of ethinyl estradiol (EE) and 120 micrograms levonorgestrel (LNG), the active ingredients, over a seven-day dosing period. The contraceptive regimen follows a standard 28-day cycle in which the patient applies the patch once weekly for three consecutive weeks, followed by a patch-free week. Twirla is packaged as one box of three patches (which comprises treatment for a single cycle), and there is also a separate replacement patch available in case of inadvertent patch removal or dislocation. Patch application is variable, as it may be utilized on the buttock, abdomen, or upper torso. The company has demonstrated a therapeutically equivalent pharmacokinetic profile with all three of these application sites¹⁶.

The patch is round and made of a soft, flexible, silky fabric. Its physical structure consists of six layers, all of which combine to measure less than one millimeter in thickness. Three layers are part of the Peripheral Adhesive System, which protects the inner layers and provides optimal adhesive qualities. Two inner layers are known as the Active Matrix, which contains the active ingredients. The final layer is the Release Liner, which contains inactive ingredients used to assist in the transport of the active ingredients across the skin. Management indicated that the chemical permeation enhancers it selected are well-known to FDA. The barrier that is formed between the Peripheral Adhesive System and the Active Matrix prevents both the active and inactive ingredients from migrating to the periphery of the patch, where they could potentially break down adhesion components or even be lost. Exhibit 5 displays the patch's components.

Exhibit 5: Twirla Patch Components

Source: Company reports¹⁷

¹⁶ <http://www.sec.gov/Archives/edgar/data/1261249/000104746914004768/a2220115zs-1a.htm> (pg 108)

¹⁷ <http://www.sec.gov/Archives/edgar/data/1261249/000104746914004768/a2220115zs-1a.htm> (pg 109)

The patch will contain laser etching for identification purposes. In the 2013 FDA complete response letter the agency asked Agile to provide additional information about its laser etching of the patch and to utilize the same etching on its clinical trial materials as on its finished product. Management believes that FDA wanted to ensure that the etching does not puncture the patch layer containing the active pharmaceutical ingredient (API), which may lead to leakage of the API outside the patch. The company has a patent protecting its API in the middle layer of the patch, and management does not believe that leakage will be an issue. Furthermore, management indicated that the Twirla trade name has been conditionally FDA approved and that its packaging artwork and logo have already been submitted and approved. There may be a final packaging approval step required post-FDA approval that could minimally slow the launch, and the company will therefore wait for final FDA approval to manufacture commercial product supply.

Twirla has ample pharmacokinetic (PK) and dosing data

Agile has conducted a number of PK trials on Twirla.

- A study evaluated the EE and LNG PK profile of Twirla to compare EE exposure as it compares to Ortho-Cyclen, a COC containing 35 micrograms of EE. The study found that maximum EE concentrations maintained with Twirla (51.3 pg/mL) were 60% lower than that of the COC (131 pg/mL), while steady state concentrations of EE from Twirla were 15-20% lower than that of the COC (35.7-37.3 pg/mL vs. 41.5 pg/mL)¹⁸, and therefore, according to FDA criteria, Twirla cannot be considered bioequivalent to Ortho-Cyclen. The study also established that the calculated daily EE dose for Twirla (approximately 30.1 micrograms) is within the range seen in COCs containing 30 micrograms EE and about half of the daily EE dose for Ortho Evra.
- Twirla was tested in a number of environmental conditions including cold water, whirlpool, treadmill, and dry sauna and drug concentrations were maintained within therapeutic ranges while adhesion remained excellent.¹⁹
- A PK study evaluating the absorption and drug concentration of the drug components in Twirla at three anatomical sites (abdomen, buttock, upper torso) found lowest drug absorption at the abdomen, though drug exposure for all sites was therapeutically equivalent.²⁰
- Agile conducted three Phase I trials and one Phase II trial of Twirla that demonstrated that the patch delivers drug levels of EE and LNG that are comparable with marketed low-dose contraceptives, and we therefore don't expect any regulatory questions surrounding dose selection for this compound.²¹

The first Phase III trial of Twirla suffered from inappropriate patient selection

A Phase III study in 1,504 women followed over 13 menstrual cycles compared Twirla to a COC containing 20 micrograms EE and 0.1 milligrams LNG, with primary endpoints of contraceptive efficacy (as defined by the Pearl Index summarized in Exhibit 6), cycle control (incidence of breakthrough bleeding or spotting), subject compliance, and safety. The sample size was based on FDA requirements of 10,000 28-day treatment cycles of exposure to the patch, with at least 200

¹⁸ Pharmacokinetic Profile of AG200-15, a Transdermal Contraceptive Delivery System, in Healthy Women. David Archer, Frank Stanczyk, Marie Foegh.

¹⁹ Pharmacokinetics and adhesion of Agile transdermal contraceptive patch (AG200-15) during daily exposure to external conditions of heat, humidity and exercise. David Archer, Frank Stanczyk, Arkady Rubin, Marie Foegh. October 5, 2012.

²⁰ Therapeutically equivalent pharmacokinetic profile across three application sites for AG200-15, a novel low-estrogen does contraceptive patch. Frank Stanczyk, David Archer, Arkady Rubin, Marie Foegh. October 31, 2012.

²¹ <http://www.sec.gov/Archives/edgar/data/1261249/000104746914004768/a2220115zs-1a.htm> (pg 99)

women completing one year of therapy.²² The subjects were required to be sexually active women between the ages of 17-40 (under 35 if smokers), with normal menstrual patterns. Study compliance was measured via paper daily diary cards and measurement of plasma drug levels. There were 96 study sites that participated in this clinical trial.

Exhibit 6: Pearl Index Definition

$$\text{Pearl Index} = \frac{\text{Number of Pregnancies} \times 12}{\text{Number of Women} \times \text{Number of Months}} \times 100$$

Source: Company reports and Cantor Fitzgerald research

In its first trial the company attempted to enroll a population that was representative of a typical patch user based on its discussions with FDA. In doing so, the trial enrolled a high number of minorities (43-44%), obese participants (33% of patients had BMI \geq 30), and new users (57% of women had no exposure to hormonal contraceptives within six months of study start). This population differed from populations enrolled in trials of previously approved CHCs as summarized in Exhibit 7 below. Patients in these trials were more experienced users of hormonal contraceptives (who are more compliant) and the trials contained fewer minorities. Though recent studies and reviews have found no convincing evidence that obese women have a higher risk of hormonal contraceptive failure, “there is some evidence that the obese population may have poorer adherence to medication.”²³ For this reason, inclusion of a high percentage of obese patients in the first Twirla trial may have also negatively skewed trial results. Agile management therefore believes that the patient population it utilized in its Phase III trial resulted in higher pregnancy rates relative to other contraceptive trials as evidenced by its stratified analysis of Pearl Index by patient group summarized in Exhibit 8.

Exhibit 7: Phase III Trial Subject Demographics

		Contraceptive Product (Year of approval)					
Hormonal Contraceptive Use:		Twirla	Seasonique (2006)	Yaz (2006)	Lo-Seasonique (2008)	Natazia (2010)	Quartette (2013)
Current Users:		18% ^a	0%	60% ^b	0%	59% ^c	0%
Within 6 months of enrollment:	Yes ^d	44%	68%	0%	61%	0%	44%
	No ^e	56%	32%	0%	39%	0%	56%
Race/ethnicity:	Hispanic	15%	5%	5%	10%	13%	11%
	Black	22%	11%	4%	12%	7%	18%

Current user definitions:

- Used hormonal contraceptive within seven days of enrollment
- Using an oral contraceptive at screening, just prior to study start
- Using oral contraceptives prior to study start

Use within six months of enrollment definitions:

- Twirla: recent and current users; Quartette/Seasonique/Lo-Seasonique: continuous users
- Twirla: new users; Seasonique/Lo-Seasonique: fresh start and prior users
- Quartette: new start and prior users

Source: Company reports²⁴ and Cantor Fitzgerald research

²² Low-Dose Levonorgestrel and Ethinyl Estradiol Patch and Pill. Andrew Kaunitz, David Portman, Carolyn Westhoff, David Archer, Daniel Mishell, Arkady Rubin, Marie Foegh. (pg 4)

²³ Trussell James, and Portman David. The creeping pearl: why has the rate of contraceptive failure increased in clinical trials of combined hormonal contraceptive pills? Contraception 88 (2013) 604-610.

²⁴ <http://www.sec.gov/Archives/edgar/data/1261249/000104746914003909/a2219692zs-1a.htm> (pg 108)

Exhibit 8: Phase III Pearl Index Stratified by Subject Demographics

	Demographic	Pearl Index
Race/ethnicity	White	3.6
	Hispanic	5.0
	Black	15.1
Previous contraceptive status	New users	8.7
	Experienced users	3.0
	Current users	0.0
Race/ethnicity and previous contraceptive use status	Hispanic subjects, new users	7.5
	Black subjects, new users	16.0

Source: Company reports²⁵ and Cantor Fitzgerald research

Based on inappropriate patient selection, investigator inexperience, and high patient noncompliance/discontinuation rates, we think the first Phase III trial attained a Pearl Index that was unacceptable to FDA.

The results of the Phase III trial were a combined Pearl Index for Twirla of 5.76 and 6.72 for the COC control arm, which were higher than the range of 1.34–3.19 found in pivotal studies conducted on products that have been approved by the FDA in the previous 10 years.²⁶ Management attributes the poor study outcome to a number of factors such as high patient drop-out rates (36.9% in patch group, 27.6% in pill group, relative to a desired 30% discontinuation rate²⁷); four study sites contributing 36% of the pregnancies in the trial; and a high percentage of patient non-adherence to study drug usage (9–13%).²⁸ Furthermore, the rate of non-compliance was three times higher amongst new users than amongst current or recent users of the patch, which further supports the idea that a high number of inexperienced patients adversely impacted the outcome of the trial. Management also believes that its contract research organization (CRO) utilized a number of sites with no contraceptive trial experience for the study that rapidly enrolled a large number of inappropriate patients, which led to a higher-than-anticipated rate of pregnancies in the trial.

²⁵ <http://www.sec.gov/Archives/edgar/data/1261249/000104746914004768/a2220115zs-1a.htm> (pg 116)

²⁶ <http://www.sec.gov/Archives/edgar/data/1261249/000104746914004768/a2220115zs-1a.htm> (pg 113)

²⁷ Low-Dose Levonorgestrel and Ethinyl Estradiol Patch and Pill. Andrew Kaunitz, David Portman, Carolyn Westhoff, David Archer, Daniel Mishell, Arkady Rubin, Marie Foegh. (pg 4)

²⁸ Low-Dose Levonorgestrel and Ethinyl Estradiol Patch and Pill. Andrew Kaunitz, David Portman, Carolyn Westhoff, David Archer, Daniel Mishell, Arkady Rubin, Marie Foegh. (pg 3)

Exhibit 9 displays previously approved hormonal contraceptive products with corresponding Pearl Indices and confidence intervals from pivotal Phase III studies.

Exhibit 9: Pearl Indices from Comparator Products

Drug	Pearl Index	Confidence Interval
Ortho Evra	1.07	0.60-1.76
Seasonique	1.34	0.54-2.75
Femcon FE	1.36	NA
YAZ	1.41	0.73-2.47
Natazia	1.64	NA-3.82
Loestrin 24 FE	1.82	0.59-4.25
Seasonale	1.98	0.54-5.03
Generess FE	2.01	1.21-3.14
Ortho-Tri-Cyclen Lo	2.36	1.33-3.40
Lybrel	2.38	1.51-3.57
Loseasonique	2.74	1.92-3.78
Lo Loestrin	2.92	1.94-4.21
Quartette	3.19	2.49-4.03

Source: Company reports and Cantor Fitzgerald research

Safety data support approval, in our view:

Twirla safety was relatively comparable to the COC pill and is summarized in Exhibit 10. Incidence of serious adverse events was approximately comparable between Twirla and the COC (1.3% vs. 1.2%, respectively). Three events in the Twirla group were considered possibly related to study drug (uncontrollable nausea and vomiting, antihistamine overdose, and thrombosis in the left subclavian vein) relative to a single event in the COC pill group (liver problem lacking diagnostic confirmation). We inquired further about the thrombosis event and learned that it occurred in an active weight lifter with a family history of clotting events who tested negative for Factor Xa. Management indicated that additional DVT events in its new Phase III trial would not be a crisis for the program.

Exhibit 10: Twirla Phase III Safety Data

Hormone Related Adverse Event	Pill	Patch	
	Cycles 1-6 (n=344)	Cycles 1-6 (n=1,043)	All Cycles (n=1,273)
Any	15.1%	16.7%	17.8%
Nausea	4.1%	4.3%	4.6%
Headache	4.7%	3.7%	3.9%
Weight increased	0.6%	1.9%	2.1%
Breast tenderness	1.5%	1.8%	2.0%
Vomiting	2.9%	1.4%	1.7%
Acne	2.3%	1.6%	1.6%
Dysmenorrhea	2.6%	1.5%	1.6%

Source: Company reports²⁹ and Cantor Fitzgerald research

²⁹ Low-Dose Levonorgestrel and Ethinyl Estradiol Patch and Pill. Andrew Kaunitz, David Portman, Carolyn Westhoff, David Archer, Daniel Mishell, Arkady Rubin, Marie Foegh. (pg 8)

Though the study results demonstrated that Twirla had a lower Pearl Index than its COC comparator, neither was in the acceptable range as specified by the FDA. Consequently, this led the agency to issue Agile a complete response letter (CRL) in February 2013 requesting additional Phase III studies, suggesting simplified clinical trial design and better test site monitoring and data collection procedures. Additionally, since receiving the CRL, further discussions with the FDA have solidified that if Twirla reaches a Pearl Index less than or equal to 3.19 (similar to Quartette) and an upper bound to the 95% confidence of 5 while maintaining safety standards seen in previous trials, the drug will be approved. Management believes that this goal is achievable by modifying its inclusion/exclusion criteria and maintaining closer oversight of its study centers (also via utilizing a more experienced CRO).

Agile expects to make a number of improvements to assure a successful outcome in its next Phase III trial:

Agile has added an experienced Chief Medical Officer to its team to assure improved oversight of its next Phase III trial. Based on FDA guidance, Agile has designed its new Phase III trial as a single-arm study (no COC comparator), which is expected to greatly reduce the complexity of data collection and analysis. The trial will enroll approximately 2,000 patients who will receive Twirla for one year at 50–70 experienced testing sites across the United States (sites with an OB/GYN principal investigator with prior contraceptive trial experience who will be selected based on performance metrics from prior trials). Patients will use an electronic diary to answer basic questions about sexual activity, use of back-up contraception, breakthrough bleeding, patch application timing, and patch adhesion. This electronic system, as opposed to the paper diaries used in previous trials, creates a simpler data collection tool for the patient and allows Agile to monitor the trial and adjudicate pregnancies in real time. Furthermore, patients who report pregnancies will receive an HCG test and ultrasound at the clinical visit to assure more thorough pregnancy follow-up. Patients will undergo a screening phase to demonstrate their ability to use the electronic diaries in order to qualify for the trial. With more accessible patient data, the company hopes to be able to rapidly locate problematic patients, early terminations, and non-compliant sites and address issues before they skew the trial outcome. Management indicated that it had interactions with FDA in October 2013 (meeting) and February 2014 (written correspondence), in which the company submitted its protocol synopsis, inclusion/exclusion criteria, study design, and statistical analysis plan and received FDA buy-in on its proposals.

Agile has secured adequate manufacturing capacity to support the launch of Twirla

Agile established an exclusive manufacturing agreement with Corium International, Inc. in 2006 to manufacture its product candidates for clinical trials as well as for commercialization. This agreement is valid until Corium has produced a “significant, agreed-upon quantity of patches, currently projected to occur no earlier than five years following the commercial launch of Twirla.”³⁰ Manufacturing takes place at Corium’s facilities in Grand Rapids, Michigan. An existing machine with capacity to produce 1.7 million patches per year has already been approved by the FDA in a pre-approval inspection in January 2013, which also allows Corium to ship patches to Europe. In preparing for scaling up production for commercialization, a new, much larger machine with capacity for 30 million patches per year has been designed and built to supply anticipated demand. The additional equipment and facilities still require FDA approval and a pre-approval inspection, but management believes that it can achieve this through an Annual Report filing to the Twirla NDA (as outlined in FDA’s guidance for scale up and post approval changes (SUPAC)) instead of having to file separately because everything remains on pre-approved premises and therefore a part of the same site license. Management projects that it may need to add a second large-capacity machine approximately four years after launching Twirla.

³⁰ <http://www.sec.gov/Archives/edgar/data/1261249/000104746914004768/a2220115zs-1a.htm> (pg 126)

Patent Estate

Agile, in partnership with Corium, developed its proprietary Skinfusion technology, which creates a soft, flexible transdermal patch that causes minimal skin irritation and has good adherence characteristics. The company believes that it has built sufficient intellectual property (IP) around its proprietary technology and product candidates, with five issued U.S. patents covering Twirla³¹ and additional IP behind its pipeline and Skinfusion technology. Exhibit 11 displays the company's patent portfolio.

Exhibit 11: Agile's Patent Portfolio

U.S. Patent #	Expiration	Description
7,045,145	Mar-21	Wet formulation of transdermal delivery prior to drying (Twirla)
7,384,650	Mar-21	Dry final product formulation of transdermal system (Twirla)
8,221,784	Mar-21	Dry final product formulation of transdermal system (Twirla/AG890)
8,221,785	Mar-21	Dry final product formulation of transdermal system (Twirla)
8,246,978	Aug-28	Structural features of transdermal system (Twirla/AG890)

Source: Company reports and Cantor Fitzgerald research

The barriers to entry of a generic in the transdermal patch space are generally believed to be stronger relative to small molecule oral agents. For example, the first generic equivalent to Ortho Evra finally made it to the market in 2Q:14, even though an abbreviated new drug application (ANDA) was filed in 2007 and bioequivalence guidance from the FDA became available in 2009. The agency recommends two studies: (1) a PK bioequivalence and adhesion study and (2) a skin irritation and sensitization study.³² Beyond running these two studies successfully, a generic competitor would also have to invest in the machinery required to produce a commercially viable number of patches, which is yet another hurdle, in our view.

We believe that the Twirla commercial opportunity is highly attractive based on historical precedent:

Ortho Evra rapidly attained a 10% share of the market before safety issues about the product emerged. We note that each share point in today's combined oral contraceptive market is valued at approximately \$100 million, which suggests that Twirla may have a \$1 billion market opportunity if it can attain similar market penetration. Furthermore, we believe that physicians will be reassured by the drug's low estrogen dose combined with the gold standard second-generation progestin, which has an excellent safety track record.

While we believe that Twirla may be subject to the same Black Box class labeling as other oral contraceptives with regard to the cardiovascular risks associated with concomitant smoking and oral contraceptive use, we do not expect Twirla to receive any unique risk language in the Black Box or its Warnings section similar to Ortho Evra regarding an increased risk of VTE and a different PK profile for Twirla relative to oral contraceptives.

Twirla offers superior tolerability to Ortho Evra and should not be impacted by the launch of Mylan's generic, in our view

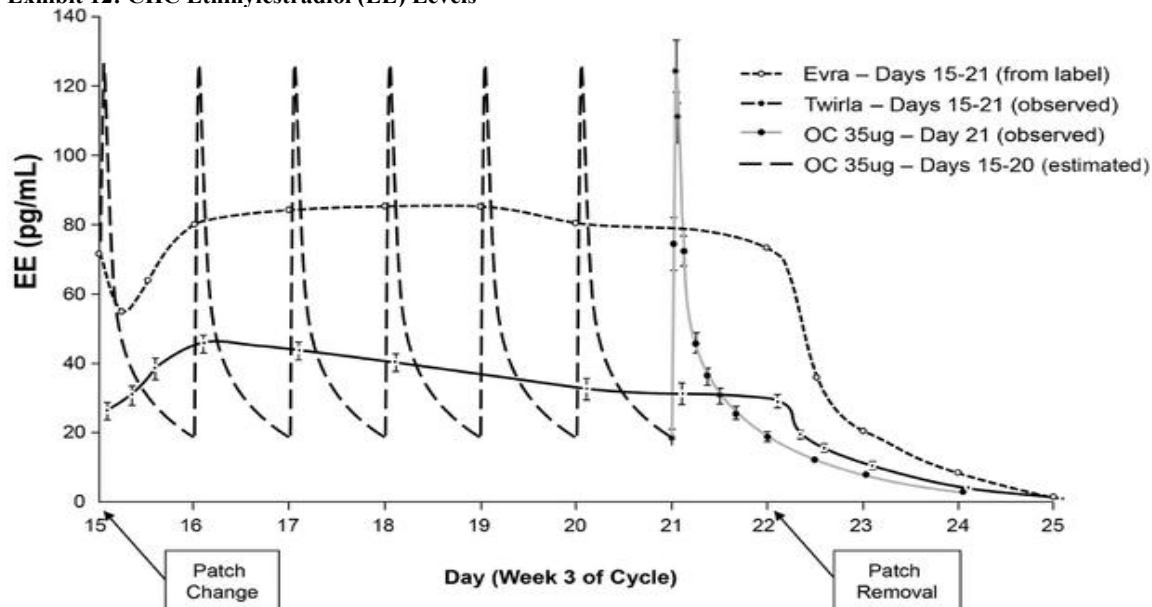
Though a direct head-to-head study of Twirla and Ortho Evra has not taken place, certain comparative metrics are available that can be used to demonstrate Twirla's superior tolerability to physicians. Exhibit 12 summarizes the distribution for average EE concentration in blood samples taken from Twirla patients in comparison to those taking Ortho Evra or an oral contraceptive regimen. It is evident

³¹ <http://www.sec.gov/Archives/edgar/data/1261249/000104746914004768/a2220115zs-1a.htm> (pg 100)

³² Draft Guidance on Ethinyl Estradiol; Norelgestromin (bioequivalence documents).

that EE area-under-the-curve (AUC) levels in those using Twirla are much lower than that found in Evra users. This difference in overall EE exposure, we believe, will ease acceptance amongst contraceptive prescribers, who decreased usage of Ortho Evra due to its increased rate of thromboembolic side effects associated with higher EE exposures.

Exhibit 12: CHC Ethinylestradiol (EE) Levels



Source: Company reports³³ and Cantor Fitzgerald research

Furthermore, Twirla use was associated with a lower incidence of adverse events in Phase III, as seen in Exhibit 13. We believe that physicians will also find these data compelling since they further illustrate the lower estrogen exposure associated with Twirla in a manner that is easily understandable to prescribers.

Exhibit 13: Adverse Event Comparison

	Twirla	Ortho Evra
Nausea	3.0%	16.6%
Breast tenderness	2.1%	22.4%
Headache	2.0%	21.0%
Application site irritation	2.4%	17.1%

Source: Company reports³⁴ and Cantor Fitzgerald research

Additionally, due to the aforementioned barrier created by the layering system used in Twirla's design, its active ingredients cannot leak to the periphery of the patch. Ortho Evra, however, does not seclude the active ingredients as well, and as a result chemicals reach the outer edges of the patch, where they can collect dust, dirt, etc. This creates a black ring around the edge of the patch, resembling that of a Band-Aid that has been worn for an extended period of time. A more clean and comfortable patch, as seen with Twirla, will be better received by both patients and prescribers, in our view.

³³ <http://www.sec.gov/Archives/edgar/data/1261249/000104746914004768/a2220115zs-1a.htm> (pg 111)

³⁴ <http://www.sec.gov/Archives/edgar/data/1261249/000104746914004768/a2220115zs-1a.htm> (pg 110)

Twirla commercialization assumptions:

- (1) We use Source Healthcare Analytics monthly retail prescription data to estimate approximately 90 million annual prescriptions for combination hormonal contraceptives. Our estimates include oral pills, patches, and NuvaRing. We believe our estimate is relatively conservative and we model minimal growth of the market, since we expect most of the new patient volume from the Affordable Care Act to be in the market by the time that Twirla launches.
- (2) We model Twirla launch in 2017, since we expect the company's response to the FDA's complete response letter to be submitted in 1Q:16 with approval in late 2016.
- (3) While we believe that the brand can attain market share levels similar to Ortho Evra (10%), we conservatively model much lower market penetration to include potential reimbursement risk associated with the Affordable Care Act.
- (4) We model 1.4 cycle packs per prescription, in-line with management guidance.
- (5) With regard to pricing, we forecast continued pricing increases in the space. Management highlighted industry price increases of approximately 8% per year in the branded segment over the past two years. Management disclosed that the Ortho Evra patch currently retails for \$110.22/cycle while Mylan's XULANE patch costs \$95.12 (a 13.7% discount to brand). If we refer to XULANE pricing and add modest 1% annual price increases, we arrive at 2017 pricing of \$98/pack. If we apply a 1.4x multiple to this price (based on packs per TRx), we generate our estimated Twirla pricing of \$137.2 per prescription.
- (6) We introduce significant gross-to-net discounting estimates to account for the presence of Mylan's generic Ortho Evra patch.

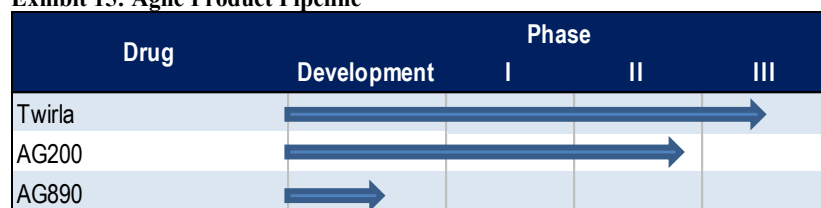
Exhibit 14: Twirla Market Assumptions (\$ in millions)

	2016E	2017E	2018E	2019E	2020E	2021E
Combined Hormonal Contraceptive Prescriptions	90,000,000	90,090,000	90,180,090	90,270,270	90,360,540	90,450,901
Twirla Market Share	0.0%	0.5%	1.5%	2.5%	3.0%	3.3%
Twirla Prescriptions	-	450,450	1,352,701	2,256,757	2,710,816	2,984,880
Packs/TRx	1.4	1.4	1.4	1.4	1.4	1.4
Price per prescription	\$137.2	\$144.06	\$151.27	\$158.83	\$166.77	\$175.11
Gross-to-net discount	35%	35%	35%	35%	35%	35%
Twirla Revenues	\$0	\$59,052,907	\$186,202,674	\$326,180,533	\$411,398,460	\$475,640,386

Source: Cantor Fitzgerald estimates and company reports

Building a pipeline of life-cycle extensions:

In addition to Twirla, Agile has two product candidates in earlier stages of development. Both of these pipeline assets leverage the company's Skinfusion technology to create additional transdermal contraceptives. AG200 is a drug that has two regimens, AG200-ER and AG200-SP. The ER formulation is designed to extend the length of the patient's menstrual cycle (no week off drug, similar to Seasonale and Seasonique, which together comprised approximately 1% of combined oral contraceptive pills at peak) and represents a new usage for the existing Twirla patch. The SP formulation provides a shortened hormone-free interval (providing less breakthrough bleeding and better mood, similar to Yaz, which attained approximately 13-14% market share of the combined oral contraceptive pills before safety concerns around drospirenone became more prominent). Both of these brand extensions would require clinical programs. Lastly, AG890 is a progestin-only formulation intended for women who are unable to, or choose not to, take estrogen. Management indicated that more early-stage work is required to take this product forward. The contraceptive market has a history of manufacturers successfully using line extensions to extend a brand.³⁵ For example, Warner Chilcott was able to preserve approximately 83% of its Loestrin-24Fe franchise via a series of line extensions such as Lo-Loestrin and Minastrin. Agile expects to use its pipeline products to extend Twirla's lifecycle and preserve revenues by extending exclusivity, thereby de-risking the threat of genericization and patent expiration. Exhibit 15 summarizes these product candidates' stages of development. Management is still evaluating next steps for this pipeline portfolio but expects to announce its next development candidate sometime in mid-2015 and to utilize a portion of its IPO proceeds to advance Twirla's next life-cycle extension program. We are not expecting Agile's pipeline to meaningfully drive revenue growth and instead view it as a means to preserve Twirla sales.

Exhibit 15: Agile Product Pipeline

Source: Company reports and Cantor Fitzgerald research

Exhibit 16 displays near-term catalysts for the company. Management expects first patient/first visit timing for the second Twirla Phase III trial in 3Q:14 with last patient/last visit in early 2016. The response to FDA's 2013 complete response letter is expected to be filed in early 2016, with a six-month review cycle, and we model product launch in 2017. As for the AG200 brand extension, management plans to announce its candidate selection and trial in 2015, with a trial start later in the year.

Exhibit 16: Upcoming Company Catalysts

Date	Product	Milestone
3Q:14	Twirla	Initiate Phase III trial
2015	AG200	Enter clinical trial
1H:2016	Twirla	End Phase III trial
1H:2016	Twirla	NDA submission
2017	Twirla	Product launch

Source: Company reports and Cantor Fitzgerald research

³⁵ <http://www.sec.gov/Archives/edgar/data/1261249/000104746914004768/a2220115zs-1a.htm> (pg. 119)

There are no direct competitive threats to Twirla in development

Exhibit 17 outlines investigational contraceptive agents that are currently being developed by other companies. The transdermal contraceptive patches from Bayer and Actavis are slightly more concerning to Agile than the oral contraceptives being developed at this time, though they don't represent direct competitors, in our view. Actavis submitted a new drug application (NDA) for its progestin-only transdermal contraceptive patch in February 2013 and received a complete response letter from the FDA which questioned differences between the patch used in clinical trials and the to-be-marketed version (different sizes/formulations). Actavis indicated on its last earnings call that it is working to prepare the data requested by the agency. Bayer's low-dose patch which uses gestodene and ethinylestradiol as its progestin and estrogen components, respectively, has completed the centralized European registration procedure. It is unknown at this time whether Bayer will pursue commercialization in the United States, but FDA has never approved a gestodene-containing product to-date. Finally, Antares' transdermal gel candidate, Nestrage, is a CHC using nesterone and 17 β -estradiol as its progestin and estrogen components, respectively. Antares is developing this product with the Population Council (an international nonprofit), and we think that it will be used to target patients in emerging markets. The companies are seeking a development partner to further advance this program.

Exhibit 17: Competitors in the Pipeline

Company	Product	Phase	Type	Estrogen	Progestin
Actavis	Transdermal	NDA	Transdermal P-only patch	NA	Norethindrone
Bayer	Transdermal	3	Transdermal contraceptive patch	EE (13 micrograms)	Gestodene (60 micrograms)
Bayer	OC	3	Pill		
Merck	OC	3	Pill		
Teva	OC	3	Pill		
Actavis	Ring	2	Vaginal Ring (Generic NuvaRing)	EE (13 micrograms)	Nesterone
Actavis	OC	2	Pill		
Antares	Transdermal	2	Transdermal gel contraceptive	Estradiol	Nesterone

Source: Company reports and Cantor Fitzgerald research

Management

Agile's team is comprised of contraceptive veterans such as Al Altomari, who launched Ortho Evra at Ortho McNeil, and Kate MacFarlane, who was responsible for women's health marketing at Warner Chilcott. In addition, management highlighted that Daniel Shames, M.D., a previous Deputy Director of the division of Reproductive and Urologic Drug Products at FDA's Center for Drug Evaluation and Research (CDER), is on its scientific advisory board. Furthermore, it has two key patch formulation experts on its team.

Exhibit 18: Agile Management

Executive	Title	Biography
Al Altomari	President, Chief Executive Officer	Mr. Altomari has served in his current position since 2010 and was Agile's Executive Chairman from 2004-2010. He is a seasoned veteran in the field, having developed and marketed several specialty pharmaceutical products at global pharmaceutical and biotechnology companies. Prior to joining Agile, Mr. Altomari was CEO of Barrier Therapeutics until it was acquired by Stiefel Laboratories. Preceding Barrier, he held several executive positions with Johnson & Johnson, namely, franchise Head of Ortho-McNeil Pharmaceuticals Women's Health Care, where he led development initiatives and successfully launched multiple products including Ortho-Evra.
Scott Coiante	Chief Financial Officer	Mr. Coiante has been with Agile since 2010. Prior to Agile, he served as VP of finance at Medarex, Inc., a publicly listed biopharmaceutical company. Before entering the industry, Mr. Coiante held management positions of increasing responsibility at Ernst & Young from 1989-2002. He holds a Bachelor's degree in accounting from Villanova University and is a certified public accountant (CPA).
Elizabeth Garner, M.D., M.P.H.	Chief Medical Officer	Dr. Garner leads the clinical research, drug safety and medical affairs teams in the clinical development of the company's pipeline. Prior to joining Agile, she was Vice President, Medical Affairs, Women's Health and Preventive Care at Myriad Genetics Laboratories and also served as a Director with both Abbott Laboratories and Merck Research Laboratories. Dr. Garner received joint M.D and M.P.H degrees from Harvard University, completed her residency in obstetrics and gynecology (OBGYN) at Brigham and Women's/Massachusetts General Hospitals, and completed a fellowship in gynecologic oncology. She is board certified in both OBGYN and gynecologic oncology.
Katie MacFarlane, Pharm.D.	Chief Commercial Officer	Ms. MacFarlane joined Agile in 2010 and is also Managing Partner of SmartPharma LLC., a pharmaceutical consulting firm. Prior to joining Agile, she was President and CEO at Xintria Pharmaceutical Corporation from 2006-2008 and Vice President of Women's Health and New Product Planning at Warner Chilcott from 2001-2006. Ms. MacFarlane received her Bachelor of Science in Pharmacy and Doctor of Pharmacy degrees from Purdue University.

Source: Company reports and Cantor Fitzgerald research

Financial Performance and Outlook

Revenues: We expect Agile to launch Twirla in early 2017 and therefore do not model any revenues until that time. We exclude any estimates for the company's line extensions at this time since we believe that these products will be utilized primarily to offset Twirla losses to generic competition rather than act as sources of incremental growth.

COGS: Management indicated that each pack of Twirla costs \$6.00 to manufacture. We expect COGS to grow to approximately \$6.65/pack by the time that Twirla launches in 2017 and therefore estimate gross margins in the 91% range for the company.

SG&A: Since Twirla is a promotion-sensitive product, we expect Agile to engage in pre-launch activities with respect to physician education in 2015-2016, and we also think the company would need to launch an aggressive campaign that appeals to both physicians and consumers. We model significant SG&A expenditure of \$55 million in 2017, which incorporates assumptions of a specialty sales force, all associated promotional activities, and samples. We expect costs to grow to include additional promotion for the company's line extensions and legal expenses in the outer years.

R&D: We expect Agile to invest approximately \$31 million in its second Phase III program of Twirla and grow this expense to account for development of the line extension portfolio as well as manufacturing expansion to accommodate Twirla growth.

Interest expense: Agile will begin to pay interest expense and principal on its \$15 million 9.2% term loan beginning in February 2015. We model complete payment of this loan in 2017 with annual principal repayments of approximately \$5 million per year.

Tax rate: We model a 39% tax rate for Agile beginning in 2018. Management estimates that it can attain profitability after a full year on the market with Twirla, which we expect to occur in 2018.

Cash: After completing its initial public offering we model net cash of \$50 million, and expect the company to have sufficient cash to complete its Phase III trial of Twirla.

Valuation

We value Agile Therapeutics via discounted cash flow analysis (DCF). We employ a weighted average cost of capital of 13% to account for the clinical risk in the program along with a 1% terminal growth rate. We use similar valuation metrics in other clinical stage companies in our universe such as Evoke Pharma and Eagle Pharmaceuticals.

Risks

- (1) Clinical risk in the conduct of the pivotal Phase III trial of Twirla and obtaining a Pearl Index that is acceptable to FDA for approval. We have risk-adjusted the probability of a positive outcome by 60%.
- (2) The Affordable Care Act may steer patients to generic forms of Ortho Evra rather than the Twirla patch.
- (3) The Twirla commercial ramp may be slower than expected.
- (4) Life-cycle extension programs carry clinical risk.
- (5) The company may need to raise additional funds in mid-2015 to finance its pipeline program.

Exhibit 19: AGRX Income Statement (dollars in millions)

	2012	2013	1Q:14A	2Q:14E	3Q:14E	4Q:14E	2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E
Revenues:														
Revenue	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	35.4	111.7	195.7	246.8	285.4
Total revenues	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	35.4	111.7	195.7	246.8	285.4
Operating expenses:														
COGS	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	2.5	7.9	14.1	18.4	22.1
Gross Profit	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	33.0	103.8	181.7	228.4	263.3
R&D	17.4	9.2	1.4	5.0	7.0	9.0	22.4	25.0	26.3	27.6	28.9	30.4	31.9	33.5
SG&A	5.9	3.6	1.1	1.8	2.1	2.5	7.5	10.0	15.0	55.0	68.8	79.1	87.0	95.7
Other	0.0	0.0	0.4	0.0	0.0	0.0	0.4	0.0	0.0	0.0	0.0	0.0	0.0	1.0
Total operating expenses	23.3	12.7	2.81	6.8	9.1	11.5	30.2	35.0	41.3	82.6	97.7	109.5	118.9	130.2
Operating income (Loss)	(23.3)	(12.7)	(2.8)	(6.8)	(9.1)	(11.5)	(30.2)	(35.0)	(41.3)	(49.6)	6.2	72.2	109.6	133.1
Interest income	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.3	0.4	0.6	0.0	0.1	0.8	0.0
Interest expense	(0.1)	(1.5)	0.0	(0.3)	(0.3)	(0.3)	(1.4)	(0.9)	(0.4)	(0.2)	0.0	0.0	0.0	0.0
Change in fair value of warrant liability	0.2	(0.1)	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	1.0
Other income (expense), net	0.1	(1.6)	0.0	(0.3)	(0.3)	(0.3)	(1.3)	(0.6)	(0.0)	0.4	0.0	0.1	0.8	1.0
Pretax Income	(23.3)	(14.3)	(2.813)	(7.1)	(9.4)	(11.8)	(31.6)	(35.6)	(41.3)	(49.2)	6.2	72.3	110.4	134.1
Tax Rate	NA	NA	NA	NA	NA	NA	NA	NA	0%	0%	39%	39%	39%	39%
Tax expense	0.0	0.0	(3.7)	0.0	0.0	0.0	0.0	0.0	0.0	0.0	2.4	28.2	43.1	52.3
Beneficial conversion charge	(0.6)	0.0	0.0											
Net income	(23.9)	(14.3)	0.8	(7.1)	(9.4)	(11.8)	(31.6)	(35.6)	(41.3)	(49.2)	3.8	44.1	67.3	81.8
Weighted average common shares (diluted)	39.5	49.5	9.7	13.5	18.6	18.6	18.6	23.6	27.6	29.0	30.4	32.0	33.5	35.2
Diluted EPS	(\$0.60)	(\$0.29)	\$0.09	(\$0.53)	(\$0.51)	(\$0.64)	(\$1.70)	(\$1.51)	(\$1.49)	(\$1.70)	\$0.12	\$1.38	\$2.01	\$2.32
Margin Analysis	2012	2013	1Q:14A	2Q:14E	3Q:14E	4Q:14E	2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E
Gross Margin	-	-	-	-	-	-	-	-	-	93.1%	93.0%	92.8%	92.5%	92.3%
COGS	-	-	-	-	-	-	-	-	-	6.9%	7.0%	7.2%	7.5%	7.7%
SG&A	-	-	-	-	-	-	-	-	-	155.2%	61.5%	40.4%	35.2%	33.5%
R&D	-	-	-	-	-	-	-	-	-	77.8%	25.9%	15.5%	12.9%	11.7%
Operating Margin	-	-	-	-	-	-	-	-	-	-139.9%	5.5%	36.9%	44.4%	46.7%
Net Income Margin	-	-	-	-	-	-	-	-	-	-138.9%	3.4%	22.6%	27.3%	28.7%
Growth (Y/Y)	2012	2013	1Q:14A	2Q:14E	3Q:14E	4Q:14E	2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E
Net Sales	-	-	-	-	-	-	-	-	-	-	215%	75%	26%	16%
SG&A	-	-40%	-	-	-	-	109%	34%	50%	267%	25%	15%	10%	10%
R&D	-	-47%	-	-	-	-	145%	12%	5%	5%	5%	5%	5%	5%
EBIT	-	-45%	-	-	-	-	-	-	-	-	-	1072%	52%	22%
Interest income (expense)	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Tax	-	-	-	-	-	-	-	-	-	-	-	1069%	53%	22%
Net Income	-	-	-	-	-	-	-	-	-	-	-	1069%	53%	22%
Diluted EPS	-	-	-	-	-	-	-	-	-	-	-	1013%	45%	16%

Source: Company reports and Cantor Fitzgerald research

Exhibit 20: AGRX Sales Estimates (dollars in millions)

	2012	2013	2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E
Products										
Twirla										
Sales	0.0	0.0	0.0	0.0	0.0	59.1	186.2	326.2	411.4	475.6
<i>Growth</i>							215%	75%	26%	16%
Risk Adjustment = 60%	60%	60%	60%	60%	60%	60%	60%	60%	60%	60%
Risk-Adjusted Twirla Sales	0.0	0.0	0.0	0.0	0.0	35.4	111.7	195.7	246.8	285.4
Pipeline										
AG200-ER										
<i>Sales</i>	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
AG200-SP										
<i>Sales</i>	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
AG890										
<i>Sales</i>	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Total Agile Revenues	0.0	0.0	0.0	0.0	0.0	35.4	111.7	195.7	246.8	285.4
<i>Growth</i>							215%	75%	26%	16%

Source: Company reports and Cantor Fitzgerald research

Exhibit 21: AGRX Balance Sheet (dollars in millions)

	2012	2013	2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E
Assets										
Current Assets:										
Cash and cash equivalents	20.0	2.1	23.6	36.9	48.7	2.6	11.2	60.8	134.5	223.6
Prepaid expenses and other assets	0.3	0.1	0.2	0.2	0.2	0.2	0.2	0.3	0.3	0.3
Total current assets	20.3	2.3	23.8	37.1	48.9	2.8	11.4	61.1	134.7	223.9
PP&E	7.0	12.0	15.9	20.2	25.0	25.0	23.8	22.6	21.4	20.1
Deferred financing costs, net	0.2	0.2	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Other assets	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Total assets	27.5	14.4	39.7	57.3	73.9	27.8	35.2	83.6	156.1	244.0
Liabilities										
Current Liabilities:										
Accounts Payable	1.1	0.7	0.8	0.8	0.8	0.9	0.9	1.0	1.0	1.1
Accrued Expenses	0.4	0.4	0.4	0.4	0.4	0.5	0.5	0.5	0.5	0.6
Loan Payable, current portion	0.0	5.1	5.1	5.1	5.1	5.1	5.1	5.1	5.1	5.1
Warrant Liabilities	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6	0.6
Total current liabilities	2.11	6.8	6.9	7.0	7.0	7.1	7.1	7.2	7.3	7.4
Loan Payable, long-term	14.8	9.8	9.8	4.8	0.0	0.0	0.0	0.0	0.0	0.0
Other liabilities	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Total liabilities	16.9	16.6	16.7	11.7	7.0	7.1	7.2	7.2	7.3	7.4
Stockholders' Equity (deficit)										
Preferred Stock	69.2	69.2	69.2	69.2	69.2	69.2	69.2	69.2	69.2	69.2
Common stock	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Additional paid-in capital	45.4	46.9	103.7	161.8	224.4	227.4	231.0	235.2	240.3	246.3
Retained Earnings (Accumulated deficit)	(104.0)	(118.3)	(149.9)	(185.5)	(226.8)	(276.0)	(272.2)	(228.1)	(160.7)	(78.9)
Total stockholders' equity	10.6	(2.2)	23.1	45.6	66.9	20.7	28.0	76.4	148.8	236.7
Total liabilities and stockholders' equity	27.5	14.4	39.7	57.3	73.9	27.8	35.2	83.6	156.1	244.0

Source: Company reports and Cantor Fitzgerald research

Exhibit 22: AGRX Statement of Cash Flows (dollars in millions)

	2012	2013	2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E
Operating Cash										
Net Income (loss)	(23.3)	(14.3)	(31.6)	(35.6)	(41.3)	(49.2)	3.8	44.1	67.3	81.8
Depreciation & Amortization	0.0	0.0	1.5	1.7	1.8	2.0	2.2	2.2	2.2	2.2
Non-cash stock based compensation	0.7	1.3	1.6	1.9	2.3	2.8	3.3	4.0	4.8	5.8
Non-cash interest	0.1	0.1	0.1	0.1	0.2	0.2	0.2	0.2	0.2	0.2
Non-cash stock bonus	0.0	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1
Change in fair value of warrant liability	(0.2)	0.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Other	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Changes in Working Capital	(0.3)	(0.3)	0.2	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Operating Cash Flow	(23.0)	(13.0)	(28.0)	(31.8)	(36.9)	(44.2)	9.6	50.6	74.6	90.1
Investing Activities										
Acquisition of PP&E	(6.7)	(4.9)	(5.4)	(6.0)	(6.6)	(2.0)	(1.0)	(1.0)	(1.0)	(1.0)
Other	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Investing Cash Flow	(6.7)	(4.9)	(5.4)	(6.0)	(6.6)	(2.0)	(1.0)	(1.0)	(1.0)	(1.0)
Financing activities										
Proceeds from issuance of term loan	15.0	0.0	0.0	(5.0)	(4.8)	0.0	0.0	0.0	0.0	0.0
Proceeds from issuance of common stock	0.0	0.1	60.0	60.0	60.0	0.0	0.0	0.0	0.0	0.0
Proceeds from issuance of preferred stock	19.3	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Proceeds from exercise of stock options	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Cash paid for financing costs	(0.2)	0.0	(1.0)	(1.0)	0.0	0.0	0.0	0.0	0.0	0.0
Costs in connection with IPO	0.0	0.0	(4.0)	(3.0)	0.0	0.0	0.0	0.0	0.0	0.0
Other	6.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Net cash provided by financing activities	40.1	0.1	55.0	51.0	55.3	0.0	0.0	0.0	0.0	0.0
Increase (decrease) in cash and cash equivalents	10.5	(17.9)	21.5	13.2	11.8	(46.1)	8.6	49.6	73.7	89.1
Cash and cash equivalents, at beginning of period	9.6	20.0	2.1	23.6	36.9	48.7	2.6	11.2	60.8	134.5
Cash and cash equivalents, at end of period	20.01	2.12	23.6	36.9	48.7	2.6	11.2	60.8	134.5	223.6

Source: Company reports and Cantor Fitzgerald research

Exhibit 23: Companies Mentioned

Company Name	Exchange	Ticker	Rating
Actavis Plc	NYSE	ACT	NC
AcelRx Pharmaceuticals, Inc.	NASDAQ	ACRX	NC
Antares Pharma, Inc.	NASDAQ	ATRS	NC
Apricus Biosciences, Inc.	NASDAQ	APRI	HOLD
Bayer AG	Xetra	BAYN-DE	NC
Corium International, Inc.	NASDAQ	CORI	NC
Eagle Pharmaceuticals, Inc.	NASDAQ	EGRX	BUY
Evoke Pharma, Inc.	NASDAQ	EVOK	BUY
Flexion Therapeutics, Inc.	NASDAQ	FLXN	NC
Heron Therapeutics Inc	NASDAQ	HRTX	NC
Hobby Lobby Stores, Inc.	NA	Private	NC
Johnson & Johnson	NYSE	JNJ	NC
Merck & Co., Inc.	NYSE	MRK	NC
Mylan Inc.	NASDAQ	MYL	NC
Nora Therapeutics, Inc.	NA	Private	NC
Ocera Therapeutics, Inc.	NASDAQ	OCRX	NC
OvaScience, Inc.	NASDAQ	OVAS	NC
Planned Parenthood Federation of America, Inc.	NA	Private	NC
Recro Pharma, Inc.	NASDAQ	REPH	NC
Revance Therapeutics, Inc.	NASDAQ	RVNC	NC
S1 BioPharma, Inc.	NA	Private	NC
Sprout Pharmaceuticals, Inc.	NA	Private	NC
Synergy Pharmaceuticals, Inc.	NASDAQ	SGYP	BUY
Teva Pharmaceutical Industries Limited Sponsored ADR	NYSE	TEVA	NC

Source: Company reports and Cantor Fitzgerald research

Company Description

Agile is a development-stage specialty pharmaceutical company focused on the women's contraceptive market. The company's lead pipeline product is Twirla, a low-dose, estrogen contraceptive patch that is expected to launch in 2017.

Disclosures Appendix

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SELL: We have a negative outlook on the stock based on our expected 12 month return relative to its risk. The expected return is based on our view of the company and industry fundamentals, catalysts, and valuation. We recommend investors reduce their position.

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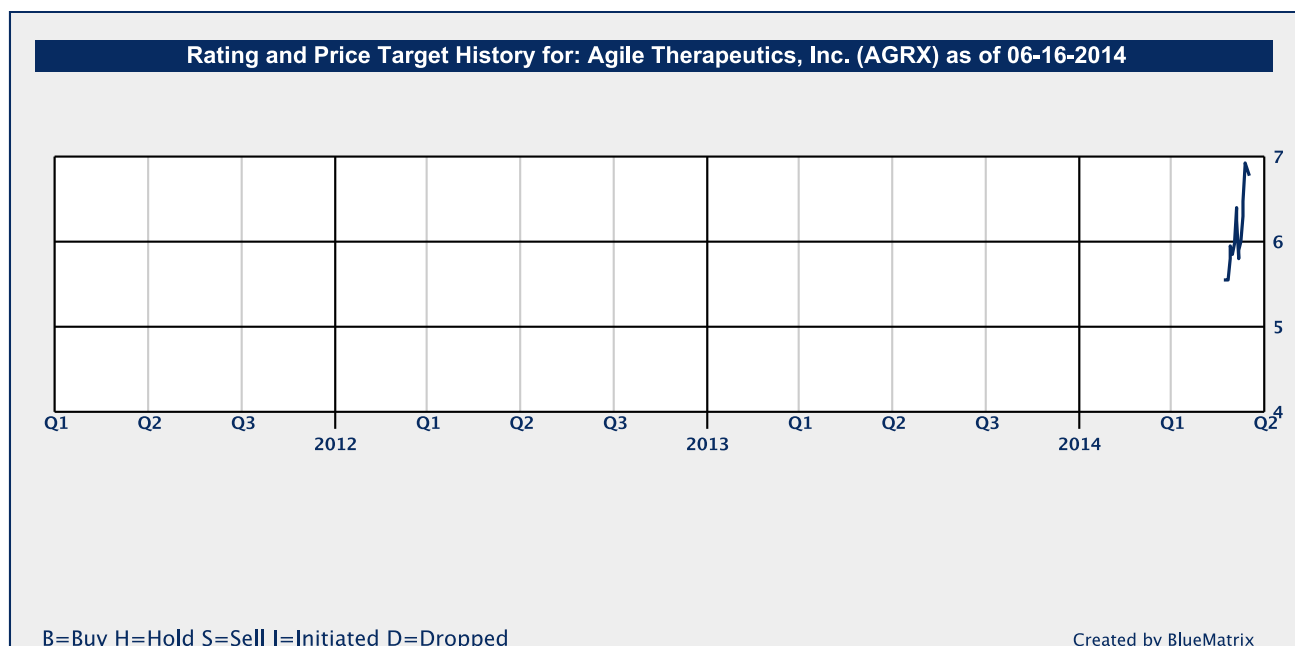
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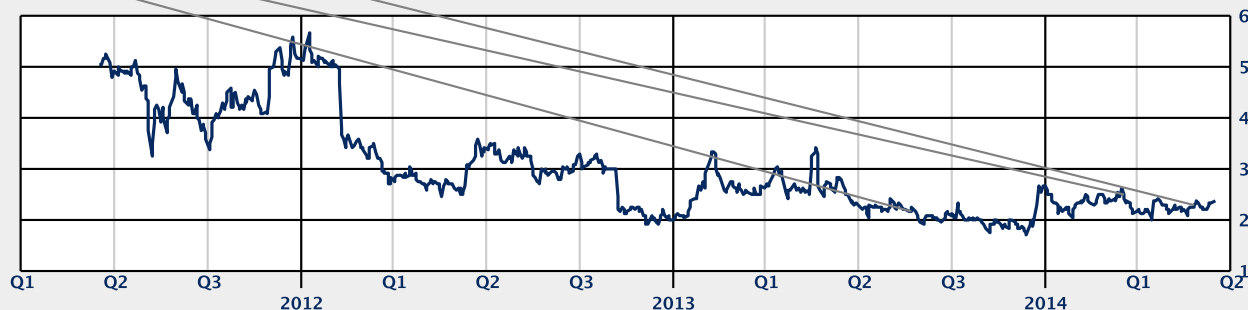


Rating and Price Target History for: Apricus Biosciences, Inc. (APRI) as of 06-16-2014

08/22/13
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03/18/14
H:\$2.5

05/27/14
B:\$3



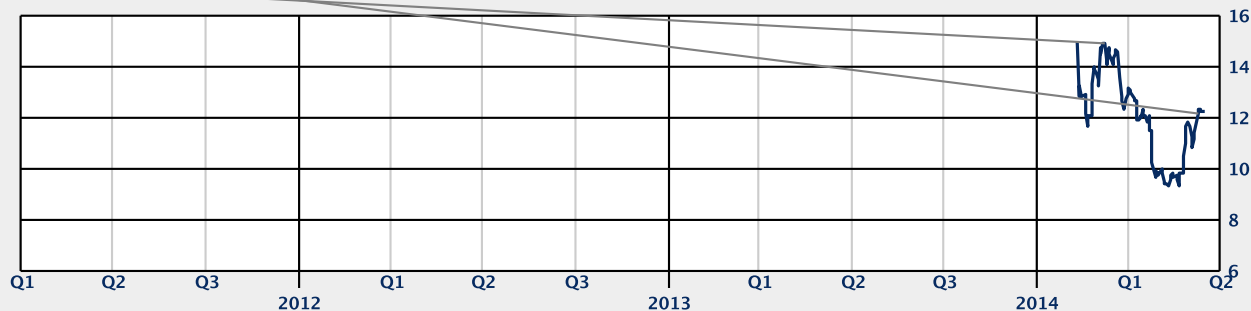
B=Buy H=Hold S=Sell I=Initiated D=Dropped

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Rating and Price Target History for: Eagle Pharmaceuticals Inc. (EGRX) as of 06-16-2014

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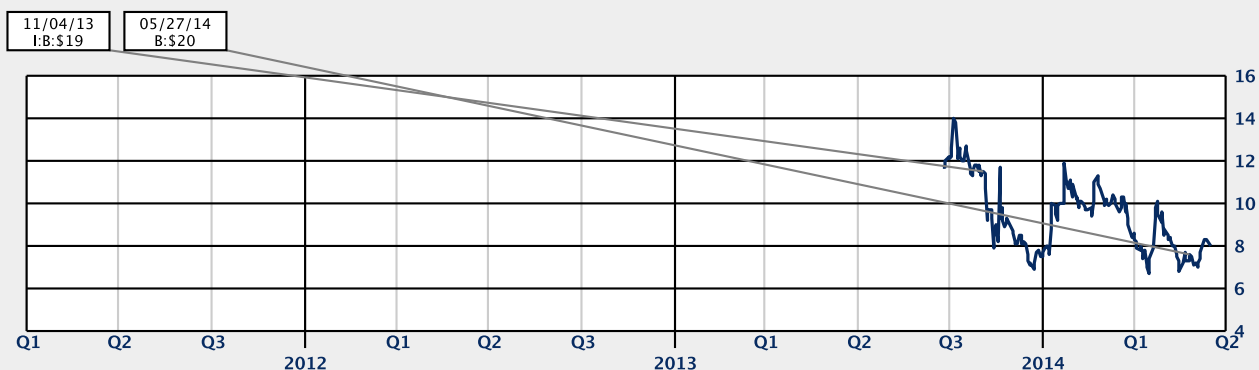
06/09/14
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B=Buy H=Hold S=Sell I=Initiated D=Dropped

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Rating and Price Target History for: Evoke Pharma, Inc. (EVOK) as of 06-16-2014



B=Buy H=Hold S=Sell I=Initiated D=Dropped

Created by BlueMatrix

Rating and Price Target History for: Synergy Pharmaceuticals, Inc. (SGYP) as of 06-16-2014



B=Buy H=Hold S=Sell I=Initiated D=Dropped

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Cantor

Rating	Count	Percent	IB Serv./Past 12 Mos.	
			Count	Percent
BUY [B]	85	58.22	22	25.88
HOLD [H]	50	34.25	7	14.00
SELL [S]	11	7.53	1	9.09