



November 19, 2013

Aerie Pharmaceuticals, Inc.

Targeting glaucoma with a new mechanism of action

Our view: We are initiating coverage with an Outperform rating and a \$20 price target. AERI is ophthalmology focused developing drugs for glaucoma. We believe AERI's product candidates could demonstrate greater efficacy, safety and convenience than currently available glaucoma drugs. Clinical results expected in 2014, 2015 and 2016 could help determine the ultimate market potential of AERI's drugs and lead to value inflection opportunities as soon as mid-2014.

Key points:

Glaucoma is an attractive therapeutic area. More than 60MM patients worldwide (2MM+ in the US) suffer from glaucoma. Branded and non-branded sales totaled \$4.5B+ in 2012. Even a modest market share in this market could result in significant product sales. We forecast peak sales of \$600-700M for PG324 and \$200-300M for AR-13324 in the US. EU sales, on which we expect AERI to receive royalties, could be \$500-600M and \$100-200M, respectively.

Novel mechanism of action from AERI. What makes AR-13324 and PG324 attractive is a novel, first-in-class mechanism of action and convenient once per day dosing, which makes them combinable with existing drugs. They could be the first drug to work on the primary drain of the eye, something not achieved successfully to date, and have greater efficacy, safety and/or convenience than currently used first and second line drugs.

Existing clinical and preclinical data shows efficacy and safety. A Phase IIb study with AR-13324 demonstrated promising IOP reduction vs. latanoprost and. Preclinical data with PG324 shows it could have better efficacy than latanoprost. Safety is clean so far. If AERI's drugs replicate these outcomes in upcoming studies they could become market leaders for the treatment of glaucoma.

Phase III endpoints are well understood. The FDA's requirements for approving drugs for glaucoma are well known, which makes it easier to gauge the efficacy and safety hurdle AERI's drugs need to reach and/or beat.

AERI retains all economics. Patent protection goes until at least 2030 and AERI owns all rights to its pipeline freeing it to commercialize on its own or partner opportunistically.

News flow is near-term and rapid. AR-13324 Phase III studies will begin in 2014 and report in 2015. PG324, which is as if not more important than AR-13324, will have Phase IIb data in 2014. The 3 month Phase III and 1 month Phase IIb efficacy endpoint is in line with industry norms for glaucoma.

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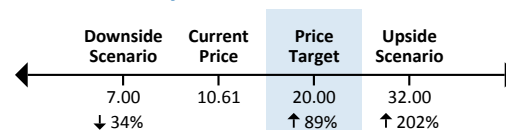
Outperform

Speculative Risk

NASDAQ: AERI; USD 10.61

Price Target USD 20.00

Scenario Analysis*



*Implied Total Returns

Key Statistics

Shares O/S (MM):	23.2	Market Cap (MM):	246
Dividend:	0.00	Yield:	0.0%

RBC Estimates

FY Dec	2013E	2014E	2015E
Revenue	0.0	0.0	0.0
EPS, Adj Diluted	(1.05)	(1.01)	(1.06)
P/AEPS	NM	NM	NM

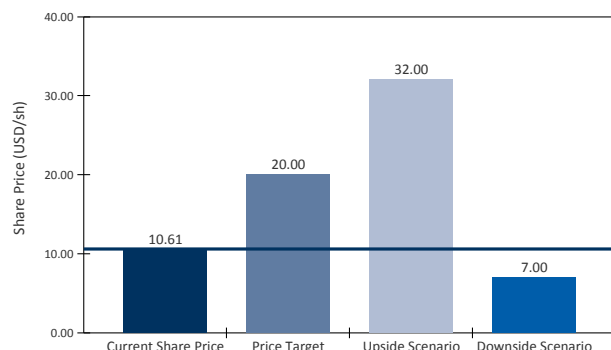
Revenue	Q1	Q2	Q3	Q4
2013	0.0E	0.0E	0.0E	0.0E
2014	0.0E	0.0E	0.0E	0.0E
EPS, Adj Diluted				
2013	(0.41)E	(0.28)E	(0.22)E	(0.22)E
2014	(0.24)E	(0.25)E	(0.26)E	(0.26)E

All values in USD unless otherwise noted.



Target/Upside/Downside Scenarios

Exhibit 1: Aerie Pharmaceuticals, Inc.



Source: RBC Capital Markets estimates

Target price/ base case

We value AERI at \$20 per share, which includes US and EU sales of AR-13324 and PG324. We assign a 60% probability of success and a value of ~\$14 per share to the US and \$6 per share to the EU opportunity. We assume a US launch in 2017 and an EU launch in 2018. We forecast peak PG324 sales of \$700-800MM and AR-13324 sales of \$200-300MM in the US and \$500-600MM and \$100-200MM in the EU, respectively. Finally, we assume patent protection through 2030 and include a terminal value based on a discount rate of 15% and a growth rate of -50%.

Upside scenario

Our upside scenario includes ~\$23 per share in value for the US opportunity and ~\$9 per share in value for the EU opportunity. We forecast peak PG324 sales of \$1.2-1.3B in the US and \$900M-\$1B in the EU and AR-13324 sales of \$200-300MM in the US and \$200-300MM in the EU. We assign products in the pipeline a 60% probability of success, a discount rate of 15%, and a terminal growth rate of -50%.

Downside scenario

Our downside scenario assumes that PG324 will not be approved in the US or EU. We value the US opportunity for AR-13324 at \$5 per share and the EU opportunity at \$3 per share. We assume market share ramps up to roughly 15% of total second-line glaucoma prescriptions in the US and 10% in the EU. Under such a scenario peak sales forecast to be \$400-500M in the US and \$300-400MM in the EU. We assign AR-13324 a 60% probability of success, a discount rate of 15%, and a terminal growth rate of -50%.

Investment summary

We believe AERI shares offer the potential for significant upside as both products in development, AR-13324 and PG324, use a new mechanism of action for the treatment of glaucoma, a blockbuster potential market. AR-13324 will enter Phase III trials based on positive Phase IIb data and PG324 a Phase IIb study based on promising preclinical data in 2014. Results from these and additional studies are expected 2014-2016. Millions of patients worldwide suffer from glaucoma, most need multiple medications, and we forecast peak sales of AERI's products at ~\$1B.

AERI owns 100% of the rights to AR-13324 and PG324 worldwide and patent protection extends into 2030, which means the company is free to partner or be acquired. Given that ophthalmology remains an attractive therapeutic area and AERI's product candidates could have a convenient, one drop once per day efficacy and safety profile, progress through clinical and regulatory milestones, as well as a partnership, could all be upside catalysts.

Potential Catalysts for AERI Shares

- **Phase IIb data for PG324 in 2014.** Important catalyst as it could show differentiation in efficacy vs. latanoprost, the current market leader.
- **Phase III data for AR-13324 in 2015.** Important catalyst as positive data could lead to an NDA and MAA filing.
- **Phase III data for PG324 in 2016.** Key catalyst as clean safety and efficacy beyond latanoprost could make PG324 the first-line drug of choice.
- **Potential partnership for AR-13324 and PG324.** AERI owns worldwide rights to both product candidates and a partnership is likely after Phase III data.
- **Potential approvals and launches in 2017 in the US and 2018 in the EU** following regulatory filings in 2016.

Risks to Our Investment Thesis

- **Pivotal Phase III and earlier stage studies could fail.** AR-13324 must show non-inferiority to a comparator over a longer period and PG324 must show a benefit in patients which raises risk of failure.
- **PG324 Phase IIb study could fail.** Our assumption for success is based on pre-clinical data with PG324 and testing it in patients increases risk.
- **AERI could fail to find a partner** for AR-13324 and PG324 outside the US.
- **Sales ramp of AR-13324 and PG324 could lag expectations** as clinicians fail to take up AERI's drugs, payers put up hurdles for reimbursing branded drugs, and cheaper generic drugs with other mechanisms hamper market penetration.



Key questions for Aerie Pharmaceuticals

Our View

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|---|--|
| 1. Are results from a 28-day Phase IIb study sufficient to advance AR-13324 into Phase III trials? | In glaucoma, the vast majority of Phase II trials measure efficacy at 28 days to determine whether a compound should advance into Phase III studies. Longer studies would be useful but rare and unusual in glaucoma signaling less confidence in the studied compound. In its Phase IIb study AR-13324 demonstrated sustained intraocular pressure reduction and clean safety. |
| 2. Is there enough data to determine if AR-13324 could be safe in a 12-month Phase III study? | The only side effect seen to date is mild to moderate hyperemia, which is transient. Historically, other rho kinase inhibitors have also shown clean safety with varying levels of eye redness as the main side effect, whose impact is cosmetic. |
| 3. Why should AR-13324 succeed when AR-12286 did not? | AR-13324 converts into two metabolites one of which is 10x more potent at inhibiting rho kinase than AR-12286 was. AR-12286 was a selective rho kinase inhibitor with a single mechanism of action. AR-13324 inhibits rho kinase and the norepinephrine transporter and exerts its effect with a dual mechanism of action. Furthermore, AR-12286 showed a loss in activity over 28 days, which is why AERI studied '286 in a 3-month study. AR-13324 has shown sustained efficacy in a 28-day study. |
| 4. Will PG324 be better than a prostaglandin? | Preclinical data shows PG324 reduces intraocular pressure more than twice as much as latanoprost alone, the gold standard. This could make PG324 the most potent glaucoma drug on the market if similar efficacy were demonstrated in clinical studies. Prior PG286 clinical data supports this hypothesis: Patients receiving PG286 did better than those getting travoprost alone. |
| 5. What if PG324 fails? Does AR-13324 have commercial value on its own? | Yes. While PG324 could be the ideal first-line drug, AR-13324 could still be the best second-line drug on the market and the one most likely to see combination use with current first-line agents. This is because AR-13324 would still possess a unique mechanism of action, something not seen in glaucoma in almost 20 years, the best convenience with one drop given once per day, a better safety profile, and/or potentially the same and more likely better efficacy than any second-line agent currently on the market. |
| 6. Can AERI's products succeed in a market dominated by generics? | Yes. The value proposition is a safe, convenient, and effective new mechanism of action that will be unique and of interest to ophthalmologists. Glaucoma is chronic and progressive with half the patients taking more than one drug, which means ophthalmologists need choices and new treatment strategies. Some patients cannot tolerate or do not want to take one or more of the currently available treatments due to side effect concerns. Finally, AR-13324 and PG324's clinical profile also make them amenable to being combined with any other glaucoma drug making them the treatment of choice by themselves or in combination regimens. |



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Portfolio manager's summary

Aerie Pharmaceuticals (AERI) is developing a new generation of medication based on a novel mechanism of action for the treatment of glaucoma. Glaucoma is a chronic, progressive disease, characterized by raised intraocular pressure (IOP), which can lead to a loss of vision and eventual blindness. It affects 60M people worldwide including more than 2M in the US. Sales of branded and generic glaucoma drugs exceeded \$4.5B in 2012 worldwide with nearly \$2B each coming from the US and EU. AERI's drugs inhibit rho kinase, norepinephrine transporter and protein kinase C to increase fluid outflow from and decrease fluid production in the eye to lower IOP. The company has reported positive Phase IIb data with AR-13324 and promising preclinical data with PG324. Next up is a Phase IIb study for AR-13324 and Phase III trials for AR-13324, with data expected in 2014 and 2015, respectively, providing a near-term path to value creation if results are positive. We forecast AR-13324 approval in 2017 and PG324 approval in 2018. Though PG324 could be the blockbuster drug as it could have the best efficacy and safety of any glaucoma medication, even AR-13324 could be a big drug as it could have the best efficacy and safety of any second-line glaucoma drug. AERI owns all rights to these drugs worldwide, which are patent protected into 2030. This leaves AERI free to commercialize the products itself, partner on a global or regional basis, and/or sell the company.

Key selling points

Unique mechanism of action targets glaucoma. AERI's compounds inhibit rho kinase (main drain of the eye), norepinephrine transporter and protein kinase C and could be the first new drugs approved with a novel mechanism of action targeting glaucoma in nearly 20 years. The products work by both increasing the outflow from the main drain while decreasing inflow into the eye. Combining AR-13324 with a 1st-line drug such as a prostaglandin would utilize the primary and secondary drains to maximize outflow as well as decrease fluid inflow into the eye.

Previously reported Phase IIb and preclinical data lowers clinical and development risk. AR-13324 showed a reduction in IOP that was: (i) Only 1 mmHg less than latanoprost, the current gold standard, showing potency as a single agent; (ii) Similar to latanoprost in patients with lower baseline IOP, and (iii) Better than currently used second-line drugs for glaucoma. Preclinical data with PG324, a single-drop combination of AR-13324 and latanoprost that is dosed once per day, showed significantly better efficacy than latanoprost alone. Safety was clean and prior programs provide further support for combining AERI's drugs with a prostaglandin.

Convenient dose and administration allows combinations. All of AERI's products are designed to be single-drops, dosed once per day, which is important as patients find it inconvenient to use eye drops multiple times per day, which reduces compliance. Given AR-13324's clinical profile, it would be easy to combine with latanoprost. It could be used as one drop each of AR-13324 and latanoprost administered once per day or in combination a single drop combination dosed once per day, which is PG324, AERI's potential first-line drug. Most glaucoma drugs are dosed multiple times per day, which makes them inefficient to combine with prostaglandins, the first-line standard of care, which are dosed once per day.

Clinical hurdles are well established and understood. The FDA expects three months of efficacy and one year of safety data. For a second line agent, the clinical hurdle is non-inferiority versus an active comparator, most likely timolol. For a first line drug, the clinical hurdle is superiority to an active comparator, most likely latanoprost.



Market is large and AERI's drugs could see first- and second-line usage. More than 60M patients worldwide suffer from glaucoma, including nearly 2M each in the US and EU. Worldwide sale for generic and branded drugs totaled ~\$4.5B in 2012 with \$1.9B in sales in the US. IMS data shows 31 million prescriptions written in the US annually (16 million prescriptions for 1st-line and 15 million prescriptions for 2nd-line drugs), which at branded drug pricing would mean a US market of ~\$3B+. Even a modest market share could mean sales in the hundreds of millions of dollars.

AR-13324 and PG324 are differentiated and could see strong uptake and high sales. AERI's products use unique mechanisms of action, target the primary and in combination secondary drains of the eye, are convenient to administer as once per day drugs, and have clean safety. Since PG324 is designed to be better than latanoprost, the current first-line drug of choice, it could become a blockbuster drug upon approval. Similarly, AR-13324 could become the 2nd-line treatment of choice given the efficacy and safety seen to date but it could even see usage 1st-line with significant sales potential by itself. Our base case forecasts total product sales of nearly \$1B, with PG324 sales of ~\$700-800M and AR-13324 sales of ~\$200-300M.

Wholly owned assets have long patent life. The composition of matter patent on AR-13324 and PG324 will expire in 2030. AERI owns worldwide rights to AR-13324 and PG324.

News flow is near-term, rapid and important in 2014-2018. AR-13324 will begin Phase III studies and PG324 will start a Phase IIb trial in 2014. Results from the Phase IIb study are expected in 2014 since the primary endpoint is measured at 1-month, Phase III study in 2015 as the primary endpoint is measured at 3-months, potentially a Phase III PG324 study and an NDA for AR-13324 in 2016. Assuming positive results, regulatory filings are expected in 2016 and 2017 followed by approvals in 2017 and 2018. We believe Phase IIb data in 2014 is as important as Phase III data in 2015.

Ophthalmology seasoned management team. AERI's Chief Executive, Chief Medical and Chief Operating officers all have significant experience developing, marketing and selling drugs for various eye disorders, including glaucoma. AERI's CEO was previously the CEO of ISTA Pharmaceuticals, an ophthalmology focused company, that was acquired by Bausch & Lomb. Furthermore, AERI's Chief Scientific Officer is one of the co-founders and its Chief Financial Officer has significant experience with reimbursement.

Risk factors

Prior attempts at developing a rho kinase inhibitors have mostly failed. Other companies developing rho kinase inhibitors have faced setbacks or discontinued development due to limited side effects, primarily hyperemia, or frequent dosing.

Limited data set compared to other indications. Glaucoma studies are advanced using 28-days of efficacy and safety data. Similarly, AERI's AR-13324 and PG324 will go into 90-day Phase III studies after completing 28-day Phase IIb studies. This increases risk as a longer-term study must replicate successful results seen in a much shorter study.

Prior programs focusing on AR-12286 and PG286 were discontinued. AR-12286, which was also a component of PG286, lost efficacy over time. AERI saw this trend in a 28-day study and then verified it in a longer three-month study. A similar decrease in potency is not seen with AR-13324 in a 28-day study.

Phase IIb and Phase III PG324 and AR-13324 studies could fail. The planned Phase IIb study for PG324 is based on preclinical data and the planned Phase III study for AR-13324 will have

its primary efficacy endpoint at three months, longer than the one-month endpoint used in the AR-13324 Phase IIb study. AR-13324 could fail to demonstrate non-inferiority to a comparator and PG324 could fail to demonstrate greater efficacy than its components.

Glaucoma market is price competitive as most products having gone generic. Initial treatment of glaucoma is adequate with existing drugs but at least half of patients require a second- or third-drug to control their glaucoma. However, most available products are available as generics, which means that AERI cannot compete on price and must differentiate AR-13324 and PG324 on efficacy, safety and/or convenience.

Sales ramp of AR-13324 and PG324 could lag expectations. We assume AR-13324 and PG324 will see usage because glaucoma is a chronic, progressive condition and physicians would be attracted to using a new mechanism of action, especially on patients who do not benefit from current drugs. However, a new mechanism of action could also lead to more cautious uptake initially inside and outside the US.

AERI must find a partner outside the US and commercialize itself in the US. Most companies competing in the glaucoma space are far larger in size and financial capabilities than Aerie Pharmaceuticals. AERI must also find a partner to commercialize AR-13324 and PG324 outside the US. A timing of such a deal and financial terms are indeterminate.

Timelines are rapid and delays could disappoint investors. AERI will initiate a Phase IIb study for PG324 in 2014, a Phase III study of AR-13324 in 2015, and a Phase III study of PG324 in 2016. AERI could also partner one or more candidates from its pipeline outside the US. Keeping up with this schedule could require flawless execution and positive data and any delay could disappoint investors and increase caution regarding execution.

Exhibit 2: Forecast news flow

Timing	Expected News Flow	Program
Early 2014	Initiate Phase IIb studies in glaucoma	PG324
1Q:14	3-month data from 6- and 9-month tox studies	AR-13324
Mid-2014	Initiate Phase III trials in glaucoma	AR-13324
Mid-2014	Phase IIb results	PG324
2014 / 2015	Final 6- and 9-month data from 2 tox studies	AR-13324
2014 / 2015	Potential ex-US partnership(s)	
Mid-2015	Efficacy results from Phase III studies	AR-13324
1H / Mid-2015	Initiate Phase III trials in glaucoma	PG324
2H:15 / Early 2016	Phase III results in glaucoma	AR-13324
2015 / 2016	Initiate Phase I trials	AR-13533
Mid-2016	File NDA	AR-13324
1H / Mid-2016	Efficacy results from Phase III studies	PG324
2H:16 / Early 2017	Phase III results in glaucoma	PG324
1H / mid-2017	Expect approval and launch	AR-13324
Mid-2017	File NDA	PG324
Mid-2018	Expect approval and launch	PG324

Source: Company reports and RBC Capital Markets estimates

**Exhibit 3: Pipeline**

Product	Mechanism	Stage	Indication
AR-13324	Dual-action ROCK / NET inhibitor	Phase III planned	Glaucoma
PG324	Triple-action ROCK / NET inhibitor and latanoprost, a PGA	Phase IIb	Glaucoma
AR-13533	Dual-action ROCK / NET inhibitor	Pre-clinical	Glaucoma

Source: Company reports

Recently completed initial public offering

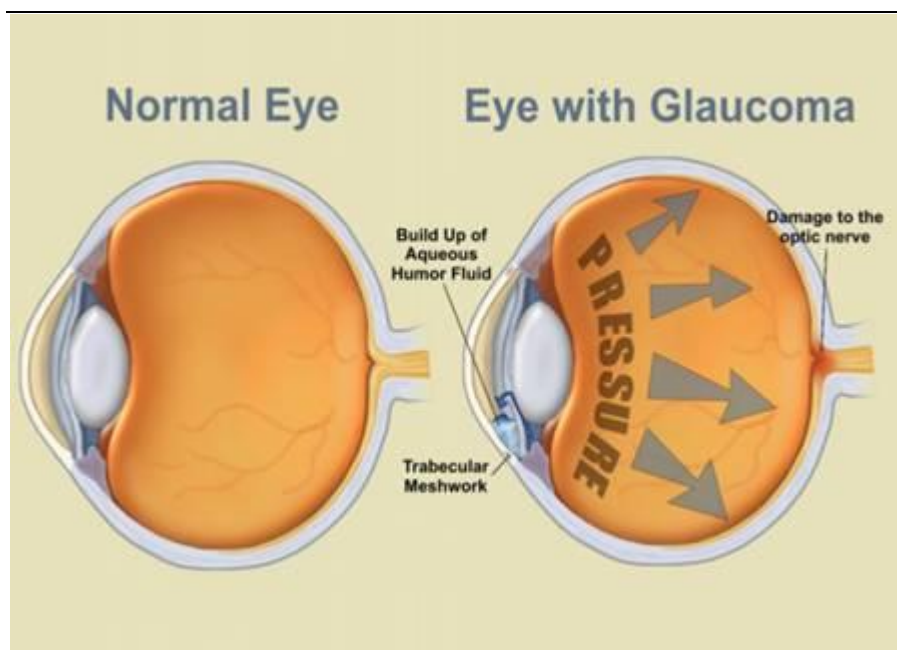
Aerie Pharmaceuticals, Inc. (AERI) completed its US initial public offering (IPO) on October 25, 2013, and exercise of the over-allotment option on October 30 to raise approximately \$68.4MM. AERI offered 6.7MM shares and an additional 1MM shares as part of the over-allotment at \$10 per share. The company ended June 2013 with approximately \$2.4MM in cash. Therefore, pro forma cash balance after the IPO is roughly \$61.4MM taking into account assumptions regarding cash used in 3Q. AERI raised capital to fund clinical trials for AR-13324 and PG324. Approximately \$34MM will be used on completing Phase III trials for AR-13324 and ~\$6MM to complete the Phase IIb study for PG324. The balance of nearly \$21MM will be used for working capital and for general corporate purposes.

Glaucoma: chronic, progressive disease that could lead to blindness

Glaucoma is a progressive chronic disease that is the second leading cause of blindness in the world. The disease requires lifelong treatment to keep intraocular pressure in check and reduce the chances of furthering nerve damage. Glaucoma is characterized by increased intraocular pressure (IOP) and damage to the optic nerve, often diagnosed by a loss in vision. The increased IOP is a result of an imbalance in fluid leaving and getting into the eye. In a healthy eye fluid is continuously produced and drained in order to maintain a pressure gradient while providing nutrition to the eye. In glaucoma, damage to the drainage networks of the eye cause a buildup of fluid, raised intraocular pressure, and damage to the optic nerve leading to deterioration in vision. Blindness can occur though is rare. While high IOP is a sign of glaucoma and potential nerve damage, patients can have nerve damage and vision loss across a wide range of IOPs.

IOP levels in healthy individuals range between 10-21 mmHg. Most patients with glaucoma are diagnosed when their IOP is only low to moderately elevated at around 26 mmHg or less. Physicians typically look at the optic nerve and evaluate the visual field when patients present with IOP greater than 21 mmHg. The goal of treatment is to ideally lower pressure to 16-17 mmHg. The key in selecting an ideal 1st-line treatment is compliance, which is improved with less frequent dosing (once per day), safety, as drugs are used chronically, and efficacy. In a typical clinical practice, IOP is measured every three months. Pressure typically goes higher at night and peaks during the early hours in the morning.

Exhibit 4: Normal eye versus eye with glaucoma



Source: Company reports

There are four classes of drugs targeting glaucoma

Currently, four major classes of drugs and their combinations target glaucoma: 1) Prostaglandins (PGA), 2) Beta-blockers (BB), 3) Alpha adrenergic agonists (AA), and 4) Carbonic anhydrase inhibitors (CAI). Patients with glaucoma receive one or more of four

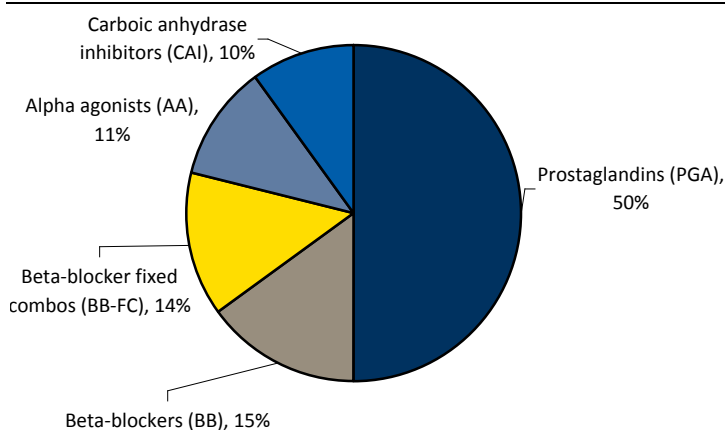
classes of drugs to keep their IOP in check. So far the newest glaucoma drugs have consisted of combinations of these different drug classes.

Prostaglandins are the most widely prescribed drug class for glaucoma with latanoprost (brand name Xalatan) the most commonly prescribed drug. IMS data shows that the share of prostaglandins as a total of all glaucoma prescriptions written is 52%-plus and has been increasing over time. There are roughly 16 million prescriptions written for prostaglandins annually in the US.

Beta blockers are the second most widely prescribed class for glaucoma and timolol (brand names Timoptic, Istalol, etc.) is the most widely prescribed beta blocker. IMS data shows that the market share for second line drugs has been declining over time with share loss greatest for beta blockers and alpha agonists while carbonic anhydrase inhibitors appear unchanged. Overall, second line drugs have been stable around 48% of all prescriptions written over the past year. There are roughly 15 million prescriptions written for beta blockers, alpha adrenergic agonists, carbonic anhydrase inhibitors, or their combinations annually in the US. Of these roughly four million prescriptions are written for beta blockers, nearly three million for carbonic anhydrase inhibitors, and approximately three million for alpha agonists. Combination regimens, such as a BB with a CAI or an AA with a CAI, largely make up the other five million prescriptions annually.

Common second line treatment strategies include (i) combining a PGA with a non-PGA (BB, AA or CAI), (ii) prescribing a non-PGA by itself, or (iii) switching to a fixed dose combination of two non-PGA drugs. Physicians can also select a surgical procedure. However, patients frequently require anti-glaucoma medication even after surgical intervention. Combinations of drug classes such as beta blockers and carbonic anhydrase inhibitors as well as carbonic anhydrase inhibitors and alpha agonists are the newest development for glaucoma treatment.

Exhibit 5: Market share of commonly prescribed glaucoma drugs



Source: Company reports



Exhibit 6: Market share of 1st- and 2nd-line drug classes over time

TRx	Jan 2013	Feb 2013	Mar 2013	Apr 2013	May 2013	Jun 2013	Jul 2013	Aug 2013
Total TRx - 1st line PGA	1,333,656	1,203,180	1,301,466	1,324,864	1,359,582	1,297,589	1,387,003	1,363,308
Total TRx - 2nd line Combo / Other	365,800	328,220	355,453	362,524	372,222	353,948	376,474	373,840
Total TRx - 2nd line BB	375,069	334,711	361,363	365,151	371,517	349,977	373,496	363,823
Total TRx - 2nd line CAI	218,340	198,784	215,365	215,243	223,160	210,162	222,618	219,947
Total TRx - 2nd line AA	291,961	262,744	283,584	287,588	293,009	276,463	292,571	288,144
Total TRx - 2nd line	1,251,170	1,124,459	1,215,765	1,230,506	1,259,908	1,190,550	1,265,159	1,245,754
Total TRx	2,584,826	2,327,639	2,517,231	2,555,370	2,619,490	2,488,139	2,652,162	2,609,062
% Share	Jan 2013	Feb 2013	Mar 2013	Apr 2013	May 2013	Jun 2013	Jul 2013	Aug 2013
Total TRx - 1st line PGA	51.6%	51.7%	51.7%	51.8%	51.9%	52.2%	52.3%	52.3%
Total TRx - 2nd line Combo / Other	14.2%	14.1%	14.1%	14.2%	14.2%	14.2%	14.2%	14.3%
Total TRx - 2nd line BB	14.5%	14.4%	14.4%	14.3%	14.2%	14.1%	14.1%	13.9%
Total TRx - 2nd line CAI	8.4%	8.5%	8.6%	8.4%	8.5%	8.4%	8.4%	8.4%
Total TRx - 2nd line AA	11.3%	11.3%	11.3%	11.3%	11.2%	11.1%	11.0%	11.0%
Total TRx - 2nd line	48.4%	48.3%	48.3%	48.2%	48.1%	47.8%	47.7%	47.7%

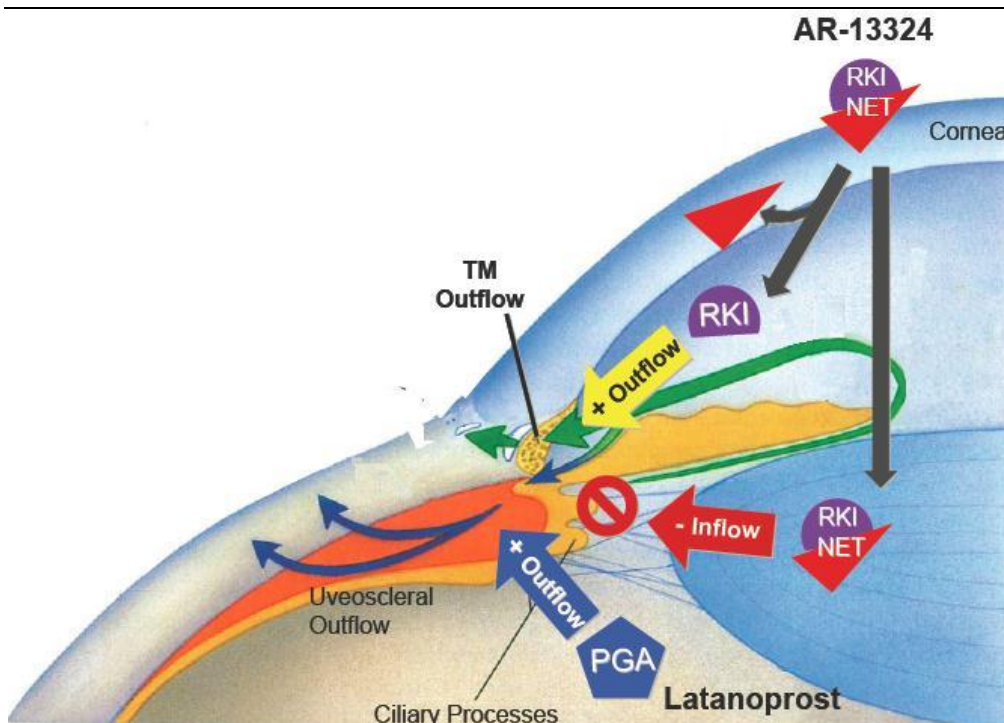
Source: IMS data

Unique mechanism of action for AERI's drugs: AR-13324 and PG324

AERI's products represent a new mechanism of action by combining rho kinase inhibition and norepinephrine transporter inhibition in a single compound. These potentially could be the first first-in-class and best-in-class drugs approved for the treatment of glaucoma that are also dosed as one drop, once per day. No new mechanism has been introduced for the treatment of glaucoma in nearly 20 years and AR-13324 and PG324 could be novel ways to lower intraocular pressure. Most new drugs have been life cycle improvements representing improved convenience, i.e., less frequent administration, better safety, i.e., less burning or foreign body in the eye sensation, or combinations of already existing mechanisms of action. AR-13324 and PG324 potentially introduce a new mechanism, best-in-class convenience, and improved efficacy in the first-line and potentially improved safety and efficacy in the second-line setting for the treatment of glaucoma.

The primary drainage mechanism of the eye is the trabecular meshwork (TM), which accounts for 80% of the fluid drainage. The uveoscleral pathway (UV) is the secondary drainage mechanism responsible for the draining the remaining 20% of the fluid. Inhibition of rho-associated protein kinase (ROCK) or rho kinase relaxes the trabecular meshwork and increases drainage through the trabecular meshwork while inhibition of the norepinephrine transporter (NET) increases adrenergic signaling and reduces fluid production. Inhibition of protein kinase C (PKC), a secondary signaling pathway, works in parallel with ROCK and NET inhibition to promote cell contraction in the trabecular meshwork thereby contributing to the ability of rho kinase inhibitors to maintain their efficacy. Previously, AERI also saw that any time its rho kinase lost activity there was also a loss in norepinephrine transporter inhibition, signaling that AERI's products require inhibition of both.

Exhibit 7: Mechanism of action impact simplified



Source: Company reports

Mechanism of action in greater detail

Activation of the rho GTPase pathway results in a cascade of molecular and cellular events that result in the contraction of smooth muscle cells in the eye. This contraction reduces aqueous drainage, causes a buildup of fluid, which in turn increases intraocular pressure. Thus, inhibiting this pathway will result in the relaxation of the smooth muscles to facilitate fluid outflow and therefore reduce intraocular pressure.

Two key players in rho kinase inhibition to reduce ocular pressure are trabecular meshwork or network (TM) and the ciliary muscle (CM). Inhibition of rho kinase in TM cells causes the relaxation of cells to increase outflow while in CM, it causes the opposite effect of decreasing outflow. Both TM and CM cells are responsible for the exit of aqueous humor; however, their responses to a rho kinase inhibitor and relaxation of their cells act in opposite directions. Overall reduction of ocular pressure arises from the level of rho kinase available within the cell and the percentage of outflow the TM or CM is responsible for. Since, TM cells express a higher level of rho kinase than CM cells, inhibiting the rho kinase pathway, results in greater relaxation in TM cells than CM cells. In addition, TM cells are responsible for 40-96% of the outflow vs. CM cells, which are responsible for only 4-60% of the outflow. The combination of greater relaxation and higher share of outflow in TM cells results in reduced ocular pressure.

The rho protein belongs to the ras GTPase family. Rho is activated when ligands bind to a transmembrane receptor and phosphorylate rho-GDP to rho-GTP. Activated rho binds rho-associated protein kinase or ROCK in the cytosol. ROCKs have three domains: 1) the N-terminal kinase domain, 2) the C-terminal pleckstrin homology domain, and 3) a coiled-coil domain. The N-terminal domain is the auto-inhibitory domain that reduces the activity of

ROCK. When activated rho is present, it binds to the coiled-coil domain of ROCK to reduce the auto-inhibitory N-terminal domain thereby increasing ROCK activity.

Downstream targets of activated ROCK are myosin light chain (MLC) phosphatase, which inhibits the contraction of actin fibers, and LIMK, which stabilizes actin filaments. ROCK inhibits the activation of MLC phosphatase and reduced activity of MLC phosphatase down contracts actin fibers. Furthermore, ROCK activates LIMP through the phosphorylation of threonine 508 on LIMK1 or threonine 505 on LIMK2 and this activation induces actin filament stabilization.

Trabecular meshwork (TM) and ciliary muscle (CM) cells contain actin and thus the contraction or non-contraction of actin filaments changes the overall shape of the cell increasing or decreasing fluid outflow. Within TM cells, low levels of activated ROCK reduces cell-cell adhesions, lower levels of myosin light chain phosphorylation (MLC), and lowered extracellular matrix protein production and thus increases aqueous humor drainage. While in CM cells the contraction leads to increased trabecular meshwork pore size and leads to increase aqueous drainage.

AR-13324: Phase IIb results reported; Pivotal Phase III trials next

AR-13324 is a once-daily, single drop that possesses a dual mechanism of action, rho-kinase and norepinephrine transporter inhibition. Phase IIb data showed sustained efficacy and a reduction in intraocular pressure inline with timolol but better than any other second-line agent in a 28-day study. Next steps are Phase III trials in 2014, likely versus timolol, a beta blocker, and top-line efficacy data by around mid-2015. Full clinical trial results could be available by year-end 2015 or early 2016. We expect an NDA filing in 2016 and currently model a launch in 2017.

Positive Phase IIb data for AR-13324

A 28-day Phase IIb study has been completed that compared AR-13324 to latanoprost, a prostaglandin and the current gold standard first-line treatment for glaucoma. Results achieved a targeted 5 mmHg drop in IOP, sustained efficacy, and clean safety.

Efficacy. AR-13324 0.02% showed a -5.6 mmHg drop in IOP from baseline to day 28 compared with a -6.8 mmHg drop for latanoprost, a prostaglandin. Of note, the drop in IOP is consistent with the drops seen with other second-line agents such as timolol and better than that seen with alpha adrenergic agonists and carbonic anhydrase inhibitors. Baseline IOPs were relatively consistent for the three arms around 26 mmHg. The drop at day 14 was -6 mmHg, -6.1 mmHg and -7.1 mmHg for '324 0.01%, 0.02% and latanoprost, respectively. The drop from baseline to day 28 was approximately -5.7 mmHg, -5.6 mmHg and -6.8 mmHg showing a rebound of 0.3 to 0.5, which is within the standard range of variability in measuring IOP.

Safety. No major adverse events were reported and none were really expected so the overall risk-benefit profile appears clean. Mild-to-moderate hyperemia was present in 24% of the patients on AR-13324 and 11% of the patients on latanoprost. This redness of the eye was transient. Across the 7-day Phase IIa and 28-day Phase IIb studies a total of 209 patients have been exposed to AR-13324 and the main adverse event is transient hyperemia (asymptomatic redness of the eye).

This Phase IIb study enrolled 224 patients with glaucoma, who received once-daily AR-13324 0.01%, '324 0.02% or latanoprost.

Exhibit 8: Phase IIb AR-13324 versus Latanoprost results

	AR-13324		Latanoprost
	0.01%	0.02%	
N	74	71	76
Efficacy			
Baseline IOP, mmHg	25.8	25.6	25.5
Day 14 IOP, mmHg	19.8	19.5	18.4
Change	(6.0)	(6.1)	(7.1)
% Change	-23%	-24%	-28%
vs. latanoprost	1.1	1.0	
Day 28 IOP, mmHg	20.1	20.0	18.7
Change	(5.7)	(5.6)	(6.8)
% Change	-22%	-22%	-27%
vs. latanoprost	1.1	1.2	
Day 14-28 IOP change, mmHg	0.3	0.5	0.3
Safety			
Hyperemia (mild/moderate)		24%	11%

Source: Company reports

Results similar to latanoprost for lower baseline IOP Patients

For patients with baseline IOPs of 22-36 mmHg, AR-13324 lowered IOP approximately 1 mmHg less than latanoprost. However, in patients with baseline IOP of 22-26 mmHg, AR-13324 and latanoprost lowered IOP by approximately the same amount. For the higher baseline IOP group latanoprost reduced IOP by -6.8 mmHg at day 28. However, for the lower-baseline IOP group, latanoprost reduced IOP by -5.9 mmHg. AR-13324 0.2% lowered IOP by -5.7 mmHg and -5.8 mmHg for the high- and low-IOP groups. This was a protocol specified analysis because prostaglandins, beta blockers, alpha adrenergic agonists, and carbonic anhydrase inhibitors all lose efficacy in normotensive or low elevated IOP patients.

This could be important because most patients (~80%) with glaucoma have baseline IOPs of 26 mmHg or less when they are diagnosed with glaucoma. Roughly 85% have baseline IOPs of 21-29 mmHg. Patients on prostaglandins lose roughly 1 mmHg in efficacy in patients with IOPs less than or equal to 26 mmHg. Similarly, timolol, a beta blocker, loses approximately 0.5 mmHg in efficacy for every 1 mmHg drop in baseline IOP. However, to date AR-13324 appears to retain its activity in normotensive or low elevated IOP patients. This could possibly lead to AR-13324 becoming the treatment of choice for patients who have low baseline IOP when they are diagnosed with glaucoma.

Exhibit 9: Phase IIb results by baseline IOP

	AR-13324	Latanoprost	AR-13324	Latanoprost
	0.02%		0.02%	
N	221		106	
Baseline IOP, mmHg	22 - 36		22 - 26	
Day 28 IOP, mmHg				
Change	(5.7)	(6.8)	(5.8)	(5.9)
vs. latanoprost	1.1		0.1	

Source: Company reports

Phase IIa study showed superiority to vehicle

A seven-day Phase IIa study in 85 patients that compared once-daily AR-13324 0.01%, 0.02%, 0.04% to placebo showed that a statistically significant decrease in mean diurnal IOP in all '324 treatment groups. The main adverse event was mild-to-moderate transient hyperemia, which is asymptomatic in nature.

Next steps remaining before Phase III start

Based on positive Phase IIb data, AERI will advance AR-13324 into Phase III trials in 2014. Before initiating the pivotal trials, AERI must complete 6- and 9-month toxicity studies results from which could be available around early 2014. We believe any risk to the toxicology studies not coming out clean is low. The doses being tested have previously been shown to be well tolerated in 28-day and 6-month ocular toxicology studies. Furthermore, AERI has conducted short-term toxicity studies before and seen results similar to those seen with other rho kinase inhibitors. Systemic toxicity studies are typically not done given the local delivery of glaucoma medication. We expect AR-13324 pivotal trials to be around mid-2014.

Phase III trial design for AR-13324

AERI will compare once-daily AR-13324 0.02% once daily in the evening to twice daily timolol, which is the most commonly used comparator in registration trials for glaucoma. The primary efficacy endpoint could be non-inferiority to timolol with a 1.5 mmHg non-inferiority margin at a majority of time points through day 90 (three-months). Therefore, top-line Phase III data could be available around mid-2015. We expect the Phase III study to enroll roughly 1,200 patients with a minimum baseline IOP of 21 mmHg and up to a maximum IOP of 26-30 mmHg. However, these could be subject to change pending discussions with the FDA and commercial considerations. IOP will most likely be measured at 8 AM, 10 AM, and 4 PM. The primary safety outcome will be evaluated at one year. We expect full trial data around year end 2015.

Exhibit 10: AR-13324 Phase III trial design

# of patients	~1,200 (in two studies)
Design	Randomized, double blind, placebo-controlled
Treatment arms	AR-13324 once daily + placebo Timolol twice-daily
Inclusion	- Open angle glaucoma (OAG) or ocular hypertension (OHT) - Mean/median IOP 21 to 26-30 mmHg
Exclusion	- Hypersensitivity to study drugs or timolol - IOP > 26-30 mmHg
Statistics	Non-inferiority with a margin of 1.5 mmHg
Primary outcome	Mean IOP reduction at 3 months
Secondary outcomes	% with IOP ≤ 18 mmHg; % with IOP reduction ≥ 25%
Start date	Mid-2014
End date	1H:16
Locations	TBD

Source: Company reports



AR-13324 approval possible in 2017; see stand-alone or combination 1st or 2nd-line use

Given that the rate limiting step for filing an NDA and MAA are one-year safety data, we expect a filing is likely in 2016 with approval possible in 2017. If the Phase III trial shows a similar five mmHg drop in patients with glaucoma, it would equal or exceed the efficacy currently seen with all non-PGA drugs on the market, including timolol. AR-13324 could see stand alone use in patients who do not tolerate prostaglandins, or in combination with prostaglandin as first or second line treatment, or in combination with beta blockers, adrenergic agonists or carbonic anhydrase inhibitors.

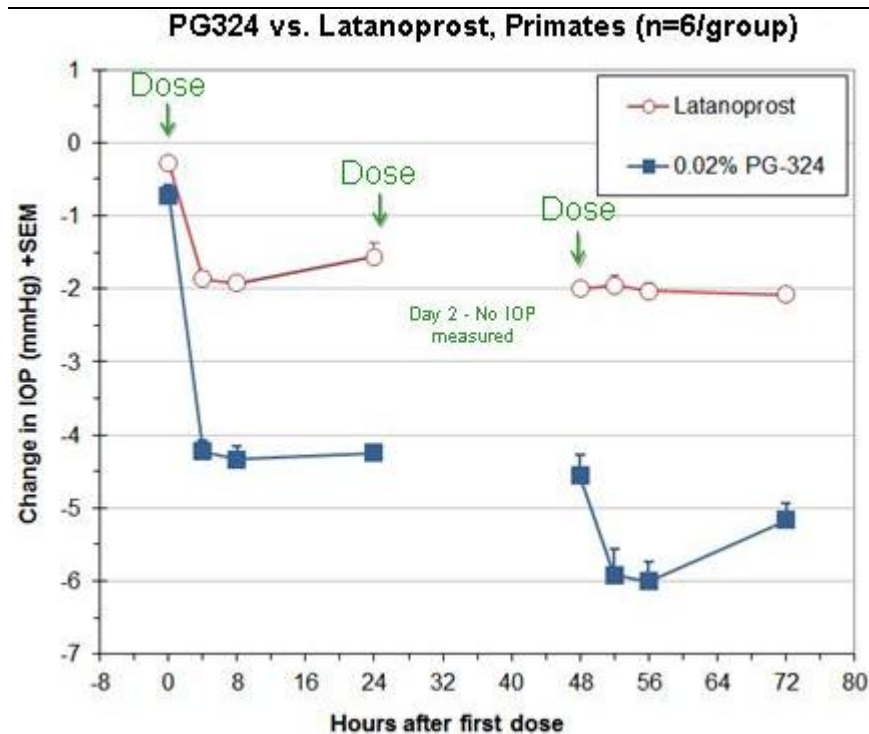
PG324: powerful efficacy in preclinical primate models; Phase IIb next

PG324, a combination of AR-13324 and latanoprost, a prostaglandin, is a once-daily, single drop that possesses a triple mechanism of action, rho-kinase and norepinephrine transporter inhibition combined with a prostaglandin. Pre-clinical data showed better efficacy than latanoprost in a primate model. Next steps are a Phase IIb trial in 2014 and a Phase III trial in 2015. Both the Phase IIb and Phase III trials would likely compare PG324 to its individual components, AR-13324 and latanoprost. Phase IIb data are expected in 2014 and Phase III data in 2016. We expect an NDA filing in 2017 and currently model a launch in 2018.

Pre-clinical data showed better efficacy than latanoprost

Results from a three-day primate model study showed that at all time points PG324 dosed once-daily reduced IOP more than once-daily latanoprost. The drop in IOP seen with PG324 was more than twice as high as the drop in IOP with latanoprost alone. Since PG324 increases drainage through the primary and secondary drains while reducing the production of fluid in the eye, we would expect better efficacy than a prostaglandin alone, which are the gold standard first-line treatment of choice but work only via the secondary drain in the eye.

Exhibit 11: Preclinical data with PG324



Source: Company reports

Prior PG286 data offers proof of concept

Though development of PG286 has been discontinued because the AR-12286 component could not maintain efficacy long term, data from a 7-day Phase II study showed the proof of principal that development of PG324 is based upon.

PG286 combined AR-12286 (0.25% and 0.5%) with travoprost (Travatan) in a fixed dose combination. Results showed that PG286 0.25% reduced IOP by 9.2 mmHg at day 7 while 0.5% reduced it by 12.2 mmHg. The reduction vs. travoprost was approximately the same for the low dose arm but much better than the travoprost alone arm for the high dose PG286 arm. Side effects were mild to moderate hyperemia where incidence was higher for the high dose arm. However, grade 2 or higher hyperemia was similar in the high dose PG286 and travoprost arms. The combination of '286 (ROCK inhibitor) with a prostaglandin also showed better efficacy than the prostaglandin alone over a 28-day treatment period providing further proof of concept for combining AERI's drugs with travoprost or latanoprost or any other prostaglandin available on the market.

Exhibit 12: Preclinical data with PG324

	PG286 0.25%	PG286 0.50%	Travoprost
N	31	29	33
Baseline IOP, mmHg	26.6 - 26.8	26.6 - 26.8	26.6 - 26.8
16 hours post 1st dose			
IOP, mmHg	17.7	15.8	18.1
Mean decrease, mmHg (%)	8.9 (33%)	11.0 (41%)	8.5 (32%)
Decrease vs. travoprost	(0.4)	(2.5)	
% Reduction vs. travoprost	4.7%	29.4%	
Day 7, 12 hours post last dose			
IOP, mmHg @ 8 AM	17.5	14.6	17.5
Mean decrease, mmHg (%)	9.2 (34%)	12.2 (46%)	9.1 (34%)
Decrease vs. travoprost	(0.1)	(3.1)	
% Reduction vs. travoprost	1.1%	34.1%	
Side Effects			
Hyperemia, mild to moderate	32.3%	58.6%	42.4%
>= Grade 2 @ day 7	0.0%	12.0%	12.0%

Source: Company reports

Next steps remaining before Phase IIb and Phase III starts

There are no further steps needed before the initiation of the Phase IIb study, which we expect to begin in early 2014. Once Phase IIb data are reported, AERI will finalize plans for the Phase III study, which we expect could start in 2015.

Phase IIb trial and Phase III design for PG324

We expect both the Phase II and Phase III trials to be similar in design with the primary differences being the number of patients enrolled and the duration of treatment. We expect both trials could compare PG324 to its individual components, AR-13324 and latanoprost. The Phase IIb and Phase III trials will be designed to demonstrate the superiority of PG324 over AR-13324 and latanoprost. The trials will enroll approximately 1,800 patients with glaucoma who have baseline IOPs of 21 mmHg and up to 26-30 mmHg. These could be modified pending further discussions with regulatory agencies.

Potential Phase IIb trial design and timelines. AERI will initiate a randomized, controlled 28-day, Phase IIb study of PG324 in approximately 300 patients in early 2014. The study will evaluate two different doses of PG324 vs. latanoprost and AR-13324 0.02%, the individual components of PG324. The primary efficacy endpoint will be superiority of PG324 to each component at 28 days. Results could read out around mid-2014 or in 2H:14.

Potential Phase III trial design and timelines. Pending positive Phase IIb data in 2014, AERI could start a Phase III trial for PG324 in 2015. The Phase III study could enroll 1,800 patients who could receive PG324, AR-13324 or latanoprost. The primary efficacy endpoint will be evaluated at 3-months while the safety data will be evaluated at 12 months. Top-line Phase III results, assuming the trial starts in 2015, could be available in 2016 with an NDA expected in 2017.

Exhibit 13: PG324 Phase IIb trial design

# of patients	~300
Design	Randomized, double blind, placebo-controlled
Treatment arms	PG324 once daily (0.01% and 0.02%) AR-13324 0.02% once-daily PG (latanoprost) once-daily
Inclusion	- Open angle glaucoma (OAG) or ocular hypertension (OHT) - Mean/median IOP 21 to 26-30 mmHg
Exclusion	- Hypersensitivity to study drugs or latanoprost - IOP > 26-30 mmHg
Statistics	Superiority to AR-13324 and latanoprost at 28 days
Primary outcome	Mean IOP reduction at 28 days
Secondary outcomes	Safety
Start date	Early 2014
End date	Mid- / 2H:14
Locations	TBD

Source: Company reports

Exhibit 14: PG324 Phase III trial design

# of patients	~1,800 (in two studies)
Design	Randomized, double blind, placebo-controlled
Treatment arms	PG324 once daily AR-13324 once-daily PG (latanoprost) once-daily
Inclusion	- Open angle glaucoma (OAG) or ocular hypertension (OHT) - Mean/median IOP 21 to 26-30 mmHg
Exclusion	- Hypersensitivity to study drugs or latanoprost - IOP > 26-30 mmHg
Statistics	Superiority to AR-13324 and latanoprost
Primary outcome	Mean IOP reduction at 3 months
Secondary outcomes	% with IOP ≤ 18 mmHg; % with IOP reduction ≥ 25%
Start date	Mid-2015
End date	1H:17
Locations	TBD

Source: Company reports

PG324 approval possible around 2018; would expect 1st-line use

Similar to AR-13324, the rate limiting step for filing an NDA and MAA are one-year safety data. We expect a filing in 2017 with approval possible in 2018. If the Phase III trial shows better efficacy than latanoprost, a prostaglandin, we expect PG324 to become the first-line agent of choice for the treatment of glaucoma.

Phase IIb results could be a major inflection point for AERI shares

Though AR-13324 presents an attractive new mechanism of action that could see usage alone or combined with first-line drugs ahead of beta blocker, carbonic anhydrase inhibitor or alpha adrenergic agonist use, PG324 with potential as a first-line drug represents the ultimate market opportunity for AERI drugs.



We believe Phase IIb data in 2014 could be a powerful signal of efficacy and commercial potential especially if PG324 demonstrates better efficacy than latanoprost. Expectations are high as PG324 could be the first drug that works through all three mechanisms of action that play a role in glaucoma versus any of the components that target only one or two of the underlying causes of increased intraocular pressure. Furthermore, PG324's better efficacy combined with similar safety and convenience to current first-line agents could make it the future standard of care if Phase IIb and Phase III results are positive.

Expect AR-13324 and PG324 to have sustained efficacy

AR-13324, a rho kinase and norepinephrine transporter inhibitor, demonstrated sustained intraocular pressure (IOP) drop over a four-week period in a Phase IIb study. Results showed a change in IOP of -6.0 mmHg at day 7 and -5.9 mmHg at day 28. The change from day 14 to day 28 was also consistent: a change from day 7-14 of -0.3 mmHg and a change of +0.1 mmHg from day 14-28. This is different from the outcome seen for AR-12286, a selective rho kinase inhibitor, whose development AERI discontinued due to a lack of sustained efficacy. In a Phase II study, the change in IOP from baseline to day 7 was -6.7 mmHg but -5.3 mmHg from baseline to day 28. This showed that AR-12286 could not sustain the drop in IOP seen at day seven.

Exhibit 15: AR-13324 maintained efficacy over a 28-day period

	Day 7	Day 14	Day 28
AR-13324 0.02% (N=71)			
Change in IOP	(6.0)	(6.3)	(5.9)
Change		(0.3)	0.4
Change vs. Day 7		(0.3)	0.1
AR-12286 0.05% (N=64)			
Change in IOP	(6.7)	(6.0)	(5.3)
Change		0.7	0.7
Change vs. Day 7		0.7	1.4

Source: Company reports

Other Rho Kinase inhibitors support single agent and sustained activity

A trial conducted by Kowa with K-115, another rho-kinase inhibitor, demonstrated a drop in IOP of 3.7 to 4.5 mmHg from baseline. A one-month study with RK1983, a Novartis product, showed a reduction in IOP of 4.4 to 4.8 mmHg vs. latanoprost of 6.6 mmHg at one month. This demonstrates that rho kinase inhibitors can have activity by themselves and could produce IOP reductions that are 2-3 mmHg less than with a prostaglandin alone. However, data is limited and from of shorter duration than the typically three-month data seen in pivotal studies with other agents.

Exhibit 16: K-115 Phase II 8-week data

Name		K-115		
Class		Rho Kinase Inhibitor		
Dose	Placebo	K-115 0.1%	K-115 0.2%	K-115 0.4%
Measure	mmHg [n]	mmHg [n]	mmHg [n]	mmHg [n]
Baseline	22.5 [54]	22.6 [53]	22.5 [54]	22.7 [49]
Week 2	-	-	-	-
Week 8	-2.5 [54]	-3.7 [53]	-4.2 [54]	-4.5 [49]
% Change	-11.1%	-16.4%	-18.7%	-19.8%

Source: Company reports

Exhibit 17: RK1983 data

Name		RK1983	Xalatan (Latanoprost)
Class		Rho Kinase Inhibitor	Prostaglandin
Dose		RK1983 0.10%	Latano 0.005%
Measure	mmHg [n]	mmHg [n]	mmHg [n]
Baseline	24.3 [73]	24.1 [71]	24.4 [73]
Week 2	-4.4 [73]	-4.1 [71]	-6.6 [73]
Month 1	-4.8 [74]	-4.4 [71]	-6.6 [73]
% Change	-19.8%	-18.3%	-27.0%

Source: Company reports

Pipeline: AR-13533 is the next-generation candidate

AERI is developing a second-generation ROCK and NET inhibitor, AR-13533, for the treatment of glaucoma. Since AR-13533 may not need enzymatic conversion prior to having activity, it could have a differentiated pharmacokinetic, pharmacodynamic, and activity profile versus AR-13324. The timing on an investigational new drug application (IND) is uncertain as AERI remains focused on developing AR-13324 and PG324 near term.

FDA's approval criteria for glaucoma drugs are well understood

The regulatory path for developing drugs for the treatment of glaucoma is well defined with clear, non-controversial endpoints that require a reduction in intraocular pressure (IOP). For drugs targeting glaucoma or ocular hypertension the FDA seeks a sustained reduction in intraocular pressure at three months as the primary endpoint. This reduction can show non-inferiority based on a pre-established non-inferiority margin to an agent already on the market or demonstrate superiority. If a drug in development is a fixed dose combination then it must demonstrate superiority to its individual components. The primary safety evaluation takes place at 12 months.



The current standards to compare against are one of four FDA approved products:

- Timolol, a beta blocker, or
- Latanoprost, bimatoprost or travoprost, which are all prostaglandins.

Most companies have developed their glaucoma products by comparing them to timolol or to latanoprost.

Competitor overview: Commercial hurdle rates for efficacy and safety

We have conducted an overview of glaucoma drugs with different mechanisms of action to assess the relative efficacy and safety hurdle AR-13324 and PG-324 would have to cross clinically and commercially. At first glance Simbrinza, the combination carbonic anhydrase inhibitor and alpha-adrenergic agonist appears to have the greatest numeric IOP reduction ability, however, unlike most other drug classes where we have two or more data points to evaluate the IOP reduction for Simbrinza is based on only one reading at three months. Combination products such as Simbrinza or even Combigan should have better efficacy than a stand-alone second-line agent based on their dual activity. Simbrinza is also dosed as a single drop, three times daily and Combigan as a single drop, twice daily, which is a less convenient dosing regimen especially versus first-line drugs on the market. Leaving Simbrinza aside prostaglandins (PGA) appear to be most potent at lowering IOP followed by beta blockers (BB), alpha adrenergic agonists (AA) and then carbonic anhydrase inhibitors (CAI). Since these are comparisons of various drugs aggregating readouts across several studies, differences in baseline patient characteristics, inclusion / exclusion criteria, and methodologies could all have had an impact on actual IOP measurements.

A more pertinent comparison when evaluating the relatively efficacy of various agents would be to look at the benefit versus latanoprost or another prostaglandin. Using this measure the reduction in IOP seen with travoprost and latanoprost appear similar, the difference between timolol and latanoprost at three months is roughly 1 mmHg worse efficacy for the beta blocker at the very least, roughly 1-3 mmHg worse efficacy for the alpha adrenergic agonist class, and 2-4 mmHg worse efficacy for carbonic anhydrase inhibitors. Efficacy is roughly 0.7 mmHg better for Simbrinza, a combination of a carbonic anhydrase inhibitor and alpha adrenergic agonist. However, data is most limited for this combination and convenience is far worse as patients must take the drug three times per day.

Exhibit 18: Select summary of efficacy data for glaucoma drug classes

Class	Prostaglandin (PGA)	Beta Blocker (BB)	Alpha-Adrenergic Agonist (AAA)	Carbonic Anhydrase Inhibitor (CAI)	Simbrinza (CAI + AAA)
Measure	mmHg	mmHg	mmHg	mmHg	mmHg
Baseline					
Month 1					
Month 3	(7.1)	(6.0)	(5.1)	(4.1)	(7.8)
Month 6					
Month 12	(6.8)	(5.5)	(3.7)	(3.3)	

Source: RBC Capital Markets

Prostaglandins appear the most powerful IOP lowering agents

Drugs such as latanoprost and travoprost appear to be the most potent at reducing intraocular pressure. On average, they lower IOP by 7.1 mmHg by month three from baseline across a select sample of studies (three data points). Actual lowering varied from 6.9 to 7.3 mmHg. In almost every case IOP lowering effect reduced from month 3 through month 12 providing further support for the need for new agents to target glaucoma. The reduction vs. latanoprost at 3 months appears similar but at 12 months latanoprost appears to have greater IOP reduction ability than travoprost. AERI is combining AR-13324 with latanoprost, the most commonly prescribed prostaglandin on the market. Prostaglandins are dosed once per day.

Exhibit 19: Select summary of efficacy data for prostaglandins

Name		Travatan (Travoprost)				Xalatan (Latanoprost)
Class		Prostaglandin (PGA)				
Dose	PGA Avg.	Travo 0.004%	vs. Latno 0.005%	Travo 0.015%	vs. Latno 0.005%	Latano 0.005%
Measure		mmHg [n]				
Baseline		25.1 [197]		24.8 [202]		25.2 [193]
Week 2		-7.5 [197]		-6.8 [202]		-6.7 [193]
Month 1		-		-		-
Month 3	(7.1)	-7.3 [197]	(0.2)	-6.9 [202]	0.2	-7.1 [193]
Month 6		-7.3 [197]		-7.0 [202]		-7.3 [193]
Month 9		-6.9 [197]		-6.5 [202]		-6.9 [193]
Month 12	(6.8)	-6.9 [197]	0.2	-6.5 [202]	0.6	-7.1 [193]

Source: RBC Capital Markets

Beta Blockers are the second most powerful glaucoma drugs

Timolol appears to lower IOP by 6 mmHg on average by month three from baseline (three data points). Reductions in IOP varied from 5.6 to 6.3 mmHg. Again, for each timolol readout there appeared to be a loss of efficacy between month 3 and month 12 further cementing the need for more treatment options for patients with raised IOP. The more pertinent comparison is IOP reduction vs. latanoprost and in this case the difference at 3 months is roughly 1 mmHg worse efficacy for beta blockers and at 12 months ~1-2 mmHg worse efficacy vs. latanoprost. Not only is relative efficacy worse than prostaglandins but beta blockers have side effects associated with them and they are largely dosed twice per day.

Exhibit 20: Select summary of efficacy data for beta blockers

Name		Istalol (Timolol)		Istalol (Timolol) Beta Blocker (BB)		Istalol (Timolol)		Xalatan (Latanoprost) PGA
Class								
Dose	BB Avg	Timolol 0.5%	vs. Latno 0.005%	Timolol 0.5%	vs. Latno 0.005%	Timolol 0.5%	vs. Latno 0.005%	Latano 0.005%
Measure		mmHg [n]						
Baseline		25.4 [195]		25.9 [368]		25.4		25.2 [193]
Week 2		-6.1 [195]		-6.1 [229]		-		-6.7 [193]
Month 1		-		-6.4 [350]		-5.6 [73]		-
Month 3	(6.0)	-6.1 [195]	1.0	-6.3 [331]	0.8	-5.6 [68]	1.5	-7.1 [193]
Month 6		-5.8 [195]		-6.3 [321]		-5.3 [67]		-7.3 [193]
Month 9		-5.6 [195]		-6.2 [153]		-4.9 [63]		-6.9 [193]
Month 12	(5.5)	-5.5 [195]	1.6	-5.9 [149]	1.2	-5.2 [61]	1.9	-7.1 [193]

Source: RBC Capital Markets

Alpha Adrenergic Agonists are the next most potent drugs

The reduction at month three from baseline in IOP with alpha agonists is 5.1 mmHg with a range of 4.2 to 5.9 (two data points; 12-month data available in only one case). With the one publication where we had 3 and 12 month efficacy for an alpha adrenergic, IOP was reduced by 4.2 mmHg at month three and 3.7 mmHg at month 12 again signaling that drugs for glaucoma lose efficacy over time. The more pertinent comparison is IOP reduction vs. latanoprost and in this case the difference at 3 months is roughly 1-3 mmHg worse efficacy for alpha adrenergic agonists and at 12 months ~3 mmHg worse efficacy vs. latanoprost. Not only is relative efficacy worse than prostaglandins but alpha agonists also have side effects associated with them and they are largely dosed two to three times per day.

Exhibit 21: Select summary of efficacy data for alpha adrenergic agonists

Name		Alphagan (Brimonidine)		Alphagan (Brimonidine)		Xalatan (Latanoprost) PGA
Class						
Dose	AA Avg.	Brim 0.2%	vs. Latno 0.005%	Brim 0.2%	vs. Latno 0.005%	Latano 0.005%
Measure		mmHg [n]				
Baseline		25.9 [460]		25.8 [232]		25.2 [193]
Week 2		-4.6 [317]		-6.6 [226]		-6.7 [193]
Month 1		-4.1 [422]		-		-
Month 3	(5.1)	-4.2 [384]	2.9	-5.9 [201]	1.2	-7.1 [193]
Month 6		-3.8 [328]		-		-7.3 [193]
Month 9		-4.2 [119]		-		-6.9 [193]
Month 12	(3.7)	-3.7 [106]	3.4	-		-7.1 [193]

Source: RBC Capital Markets

Carbonic Anhydrase Inhibitors have the least potency

Carbonic anhydrase inhibitors reduced IOP by 4.1 mmHg at month three with a range of 3.3 to 5.2 mmHg (three data points; 12-month data available in two cases). Again the signal for a reduction in benefit over time is there with 12 month data showing higher IOP readings than 3 month readouts. The more pertinent comparison is IOP reduction vs. latanoprost and in this case the difference at 3 months is roughly 2-4 mmHg worse efficacy for carbonic anhydrase inhibitors and at 12 months ~4 mmHg worse efficacy vs. latanoprost. Not only is

relative efficacy worse but carbonic anhydrase inhibitors are largely dosed two to three times per day making them less convenient than prostaglandins.

Exhibit 22: Select summary of efficacy data for carbonic anhydrase inhibitors

Name		Azopt (Brinzolamide)		Azopt (Brinzolamide)		Azopt (Brinzolamide)		Xalatan (Latanoprost) PGA
Class		Carbonic Anhydrase Inhibitor (CAI)						
Dose	CAI Avg.	Brinz 1% 2x	vs. Latno 0.005%	Brinz 1% 3x	vs. Latno 0.005%	Brinz 1%	vs. Latno 0.005%	Latano 0.005%
Measure		mmHg [n]						
Baseline		25.1		26.1		26.0 [229]		25.2 [193]
Week 2		-		-		-5.3 [227]		-6.7 [193]
Month 1		-3.5 [140]		-3.6 [138]		-		-
Month 3	(4.1)	-3.3 [138]	3.8	-3.8 [128]	3.3	-5.2 [213]	1.9	-7.1 [193]
Month 6		-3.9 [130]		-3.5 [128]		-		-7.3 [193]
Month 9		-3.3 [124]		-3.1 [121]		-		-6.9 [193]
Month 12	(3.3)	-3.2 [126]	3.9	-3.4 [121]	3.7	-		-7.1 [193]

Source: RBC Capital Markets

Combination products have stronger efficacy but retain their baggage; More proof-of-concept for AERI's drugs

Simbrinza is a fixed dose combination of a carbonic anhydrase inhibitor and an alpha adrenergic agonist. It is the most recently approved drug for glaucoma. Potency appears in line to even better than prostaglandins. However, Simbrinza comes with all the side effects associated with these two drug classes and it is dosed three times per day, making it significantly less convenient for patients than once per day combinations. Mechanistically, a carbonic anhydrase inhibitor and an alpha adrenergic agonist both decrease fluid production so together they could have synergistic efficacy. Combigan is a combination of a beta blocker and alpha adrenergic agonist. We estimated potency based on data on the label and it appears in line with a prostaglandin. However, Combigan is accompanied with all the side effects and contraindications associated with a beta blocker and alpha adrenergic agonist and it is dosed two times per day.

In our view, the stronger efficacy seen with these combinations is further proof-of-concept for potential better efficacy with AR-13324 and latanoprost, a prostaglandin. Of note, both combination products demonstrate a better efficacy than their individual components. In the case of PG324 (AR-13324 + latanoprost), the safety profile has been relatively clean and side effects even with the combination is expected to result in possibly higher hyperemia instead of any systemic side effects.

Exhibit 23: Select summary efficacy data for combination carbonic anhydrase inhibitor and alpha adrenergic agonist

Name	Simbrinza CAI + AA		Xalatan (Latanoprost)
Class	vs. Latno 0.005%		Latano 0.005%
Dose			
Measure	mmHg [n]		
Baseline			25.2 [193]
Week 2			-6.7 [193]
Month 1			-
Month 3	(7.8)	(0.7)	-7.1 [193]
Month 6			-7.3 [193]
Month 9			-6.9 [193]
Month 12			-7.1 [193]

Source: RBC Capital Markets

Differentiated mechanism, convenience, safety and efficacy all provide advantages for AR-13324 and PG324

Aside from possessing the first new mechanism of action targeting glaucoma in nearly two decades, AR-13324 and PG324 could also differentiate themselves on 1) convenience, 2) safety, and 3) efficacy versus all four drug classes currently used to treat glaucoma. AERI's drugs would be once per day, safe and with potentially better efficacy than first or second line agents or with at least the same efficacy but better safety and convenience than existing second line drugs for glaucoma.

Convenience. AR-13324 and PG324 are dosed as one drop, once per day. Though prostaglandins are dosed once per day, most second-line agents must be given more than once per day and up to three times per day. This makes AERI's drugs the idea agents to combine with either prostaglandins or other anti-glaucoma drug classes.

Efficacy. Since AR-13324 can be dosed once per day, it is likely combinable with prostaglandin and able to show better efficacy than a prostaglandin alone. Prostaglandins are the gold standard of anti-glaucoma treatment. Hence, PG324 has the potential to be the most potent anti-glaucoma agent on the market. AR-13324 has already demonstrated better efficacy than most second line agents.

Safety. Based on data generated by AERI so far as well as from prior development efforts for rho kinase inhibitors it is expected that the safety profile of AR-13324 and PG324 should be fair clean. The side effect seen most commonly is hyperemia or redness of the eye, which is transient and goes away by morning in most patients assuming they use AR-13324 or PG324 before going to bed.

Mechanism of action. AERI's drug candidates work via rho kinase and norepinephrine transporter inhibition. While rho kinase increases fluid outflow through the primary drain of the eye, norepinephrine transporter inhibition reduces fluid production. When combined with a prostaglandin fluid drainage through a secondary drain of the eye is also added. Together, they would target all the mechanisms to control fluid inflow and outflow in the eye while currently available drugs only work on fluid outflow or fluid inflow.

Exhibit 24: Competitive profile of glaucoma drug classes

Anti-Glaucoma Drug Class	Products	Peak Sales (US / EU)	Dosing / Day	Efficacy	Safety
PGA (1st-line)	Xalatan, Lumigan, etc.	\$1.7B	1x	High	Hyperemia, iris color
BB (2nd-line)	Betimol, Timoptic, etc.	>\$500M	2x	Moderate	Cardiopulmonary contraindication
CAI (2nd-line)	Trusopt, etc.	>\$500M	2-3x	Low	Sulfonamide contraindication, bitter taste
Alpha agonist (2nd-line)	Alphagan	>\$400M	2-3x	Low	Allergy, drowsiness

Source: Company reports

Side effects associated with drugs currently used to treat glaucoma

Prostaglandins. Although prostaglandins do not have any systemic side effects, they have been known to cause pigmentation of the iris and to make eyelashes grow longer. Hyperemia is also a common side effect. Pigmentation is more a cosmetic than clinical problem. However, some patients with lighter colored eyes do not want to have the color change if they have an option for an alternative. Patients with increased pigmentation have also shown higher visual field defects, cataracts, and hyperemia.

Non-prostaglandins. Not only are beta blockers, carbonic anhydrase inhibitors, and alpha adrenergic agonists given two or three times per day, they also have side effects associated with them. These include lethargy, blurred vision, reduced heart rate, unusual taste, and allergic reactions, amongst others.

- **Beta blockers.** Drugs that belong to the beta blockers class have both side effects and contraindications. Contraindications include heart failure and asthma and warnings include diabetes and obstructive pulmonary disease among others. Of all the drug classes beta blockers have the most contraindications listed. An important risk is the potential for tachycardia, which becomes of even greater concern in elderly patients and those with compromised heart function. These are typically dosed twice per day.
- **Alpha adrenergic agonists.** Use can be associated with severe allergies and conjunctivitis in some patients. Compared to beta blockers, such as timolol, there is greater blurred vision, burning and stinging sensation, and hyperemia. A higher proportion of patients also report dry mouth, fatigue and headache. Warnings on the label include patients with severe cardiovascular disease. These also have to be dosed three times per day.
- **Carbonic anhydrase inhibitors.** On label warnings include hypersensitivity reactions, severe renal impairment and corneal endothelium cell loss. The most common side effects are potential conjunctivitis and a change in taste. Carbonic anhydrase inhibitors are typically dosed two to three times per day.

Exhibit 25: Side effects, warnings and contraindications with current glaucoma drugs

Product (class)	Contraindication	Warnings
Alphagan (alpha adrenergic agonist)		
	Hypersensitivity to any component of this product	Potential of Vascular insufficiency
	Neonates and Infants (under the age of 2 years)	Severe cardiovascular disease
		Contamination of topical ophthalmic products after use
Azopt (carbonic anhydrase inhibitor)		
	Hypersensitivity to any component of this product	Sulfonamide hypersensitivity reactions
		Corneal endothelium
		Severe renal impairment
		Acute angle-close glaucoma
		Contact lens wear
Istalol (beta blocker)		
	Bronchial asthma	Cardia failure
	History of bronchial asthma	Obstructive pulmonary disease
	Severe chronic obstructive pulmonary disease	Major surgery
	Sinus bradycardia	Diabetes mellitus
	Second or third degree atrioventricular block	Thyrototoxicosis
	Overt cardiac failure	
	Cardiogenic shock	
	Hypersensitivity to any component of this product	
Simbrinza (alpha adrenergic agonist and carbonic anhydrase inhibitor)		
	Hypersensitivity to any component of this product	Sulfonamide hypersensitivity reactions
	Neonates and Infants (under the age of 2 years)	Corneal endothelium
		Severe renal Impairment
		Acute angle-close glaucoma
		Contact lens wear
		Severe Cardiovascular disease
		Severe hepatic imparement
		Potential of vascular insufficiency
		Contamination of topical ophthalmic products after use
Travatan (prostaglandin)		
	None	Pigmentation
		Eyelash changes
		Intraocular inflammation
		Macular edema
		Angle-closure, inflammatory or neovascular glaucoma
		Bacterial keratitis
		Use with contact lenses
Xalatan (prostaglandin)		
	Hypersensitivity to any component of this product	Changes to pigmented tissues
	Hypersensitivity to latanoprost	
	Hypersensitivity to benzalkonium chloride	

Source: Company reports and prescribing information

Drugs in development are existing combinations or inconvenient

The overall competitive landscape also appears favorable to AERI's products as most new drugs in development are combinations from existing drug classes, which may provide a boost to efficacy but do not address the side effect or multiple doses per day issues associated with them at this time. Most drugs in development that are dosed once per day remain prostaglandins, which is similar to the competitive dynamics currently in place for the glaucoma market. Furthermore, the rho kinase inhibitors we see also do not appear as potent as AERI's products and are dosed multiple times per day.

Exhibit 26: Competitive profile of glaucoma drugs in development

Compound	Company	Stage	Class	Administration	Comments
BOL-303259	Valeant (Bausch & Lomb)	Phase III	PGA	1x	NO-donating latanoprost
Latanoprost/ Brinzolamide	Adapt Produtos Oftalmológicos	Phase III	PGA+CAI	1x	
Latanoprostene bunod	Bausch & Lomb	Phase III	PGA	1x	
Bimatoprost/ brimonidine/ timolol	Allergan	Phase III	PGA+AA+BB	2x	Triple combination
Travoprost	Alcon	Phase III	PGA	1x	Pediatric Glaucoma Patients
Ranibizumab	Novartis	Phase III		1 injection as needed	Rare Vegf Driven Ocular Disease
K-115	Kowa	Phase III	ROCK inhibitor	2x	ROCK inhibitor; Filed in Japan
AR-13324	Aerie Pharmaceuticals	Phase III planned	ROCK/NET inhibitor	1x	ROCK/ NET inhibitor
PG324	Aerie Pharmaceuticals	Phase IIb planned	ROCK/ NET inhibitor/ PGA	1x	ROCK/NET inhibitor with a prostaglandin
DE-117	Santen	Phase IIa	PGA	1x	EP2 agonist
AMA0076	Amakem	Phase IIa	ROCK inhibitor	2x	ROCK inhibitor
Bimatoprost/ brimonidine	Allergan	Phase II	PGA+AA	2x	Dual combination
SYL040012	Sylentis	Phase II	Beta blocker	2x	RNAi beta blocker
INO-8875 (trabodenasol)	Inotek	Phase II	Adenosine agonist	2x	Adenosine A1 agonist
Vision5	ForSight Vision5	Phase II		2x	
Bimatoprost/ brimonidine	Allergan	Phase II	PGA+AA	2x	Dual combination
CF101	Can-Fite BioPharma	Phase II		2x oral	
ALZ-1101	Alleanza Pharm	Phase II		1x	
Lumigan (Bimatoprost; new formulation)	Allergan	Phase I/II	PGA		
LX7101	Lexicon	Phase I/II	LIMK2 inhibitor	Twice daily	LIMK2 inhibitor; fluid outflow through TM
MRZ-99030	Merz Pahrn GmbH	Phase I		3x	
OTX-Tp	Ocular Therapeutix, Inc	Phase I		3-4 ug daily	
ONO-9054	Ono	Phase I	PGA	1x	FP/EP3 agonist

Source: Company reports

Long patent life and wholly owned asset

AERI owns all rights to AR-13324 and PG324 giving it maximal flexibility in either marketing the drugs itself in the US, partnering them regionally or globally or having the company acquired outright if trials are positive and commercialization is successful. We currently expect AERI to find a partner outside the US.

AERI's compounds are protected with a composition of matter patent through at least 2030.

Large market opportunity: Attractive potential as 1st and/or 2nd line drugs

Global sales of generic and branded drugs targeting glaucoma totaled \$4.5B in 2012. According to the Glaucoma Research Foundation, roughly 2.2 million Americans have glaucoma. In the US, nearly 31 million prescriptions will be written for glaucoma drugs in 2013, up +5.3% from the ~28.5 million prescriptions written in 2012. Of these, roughly 16 million prescriptions (+2.9% over 2012) are for prostaglandins, the 1st-line drug class of choice, and the remaining 15 million prescriptions (+0.9% over 2012) are for drugs largely reserved for second-line use. Similarly, the number of non-prostaglandin prescriptions are roughly half of all prescriptions in the EU as well. The number of prescriptions coincide with the number of patients in the US, giving us confidence in our market forecasts. Patients require life-long treatment, as the disease is chronic and progressive. Nearly half the patients

are on more than one drug to treat glaucoma, which means there is a significant opportunity for AR-13324 to be taken up in the second-line market.

Both AR-13324 and PG324 are designed to work as one drop, once-per-day drugs. This allows for maximal convenience and flexibility in combining them with drugs currently on the market that are dosed one or more times per day. Roughly 10-15% of patients on prostaglandins do not respond to treatment. Another 10-15% of patients could have low tension glaucoma, where IOP is less than 21 mmHg yet patients continue to have optic nerve damage and visual field deterioration.

We see six paths to use for PG324 and AR-13324 in patients with glaucoma:

1. PG324 as a stand-alone, first-line treatment (one drop, once per day), including patients with low tension glaucoma, who could be low hanging fruit;
2. PG324 in combination with non-AR-13324 second-line agents (two or more drops, twice per day);
3. AR-13324 as a stand-alone, second-line treatment (one drop, once per day), especially for those patients who cannot tolerate or do not want prostaglandins;
4. AR-13324 in combination with prostaglandins as a first- or second-line combination regimen (two drops, once per day);
5. AR-13324 in combination with second-line drugs (two or more drops, twice per day); and
6. AR-13324 or PG324 usage for low tension glaucoma patients.

In addition to the clinical attributes that are favorable, there are two reasons why we believe both AR-13324 and PG324 could have high sales potential in the glaucoma market: 1) Prior to their patent expiration, the most commonly prescribed non-PGA drugs each had \$400MM in global sales and PGA drugs had >\$1B in global sales, and 2) Despite the presence of generic latanoprost, sales of Lumigan, a branded prostaglandin, totaled \$623M in 2012 (up from \$612M in 2011), which shows ophthalmologists respond to detailing, especially if it is accompanied by a different profile for a drug.

Exhibit 27: Sales of select prostaglandin and non-prostaglandin drugs

Product	Drug Class	Company	Patent Expiration	Sales (\$ in millions)		
				2010	2009	2008
Xalatan	PGA	Pfizer	2011	1,749.0	1,737.0	1,745.0
				2012	2011	2010
Lumigan	PGA	Allergan	2014	622.6	612.0	526.0
				2012	2011	2010
Alphagan P, Alphagan and Combigan	AA and AA+BB	Allergan	2012	453.2	419.4	401.6
				2008	2007	2006
Cosopt/ Trusopt	BB+CAI and CAI	Merck	2008	781.2	786.8	697.1

Source: Company reports



AR-13324 could be attractive as a 2nd-line agent with potential for 1st-line usage

We estimate AR-13324 could launch in 2017 and gain up to 15% of the total second-line market prescriptions by 2020 when sales of PG324 start reducing AR-13324 usage. We expect a 7.5% share of the second line prescription market starting in 2023. Assuming branded drug prices of ~\$100 per prescription, which is in line with what branded drugs for glaucoma have cost historically, and a gross to net adjustment of 20%, annual sales could total \$6.5MM in 2017, increase to \$235.5MM in 2020, the third full year on the market in the US, decline to \$142.6MM in 2023. In the EU, we forecast sales of \$88.2MM in 2018, \$273.5MM in 2020, and \$143.7MM in 2023. Assuming a royalty of 17.5% in the EU, revenues to AERI would be \$15.4M, \$47.9MM, and \$25.1MM, respectively. Even a small market share could result in a sizeable dollar opportunity. Our downside scenario which assumes no approval for PG324 forecasts US AR-13324 sales of \$400-500MM and EU sales of \$300-400M assuming peak market shares in the second line markets of 15% and 10% respectively.

PG324 could be the ideal 1st-line drug with blockbuster potential

The key for PG324 would be efficacy better than latanoprost or prostaglandins in general, which are the first-line treatment of choice for glaucoma, given their efficacy and relative safety and convenience vs. other drugs. We assume PG324 would ramp up moderately and eventually capture 24% of total first-line prescriptions in the US and 16% of total first-line prescriptions in the EU. Assuming a price of \$100/prescription and a gross to net adjustment of 20%, annual sales could be \$7.5MM in 2018, \$101.8MM in 2020, and \$410.9MM in 2023 in the US. We forecast sales of \$38.8MM in the EU in 2019, \$118.2MM in 2020 and \$414MM in 2023. Assuming a royalty rate of 17.5%, revenues to AERI would be \$6.8M, \$20.7MM, and \$72.5MM, respectively. Since PG324, assuming success in clinical trials, would be better than any product on the market our forecasts could prove conservative over time.

Low tension glaucoma could be another opportunity

Up to 20% of patients can have low tension glaucoma, which means despite having intraocular pressure lower than 21 mmHg they have symptoms of glaucoma. AR-13324 and potentially PG324 could show a retention of benefit vs. other market agents in patients with glaucoma who do not have elevated IOP. Results the Baltimore Eye Survey published in 1991 showed that more than 78% of patients have baseline IOP of 26 or below when first diagnosed with glaucoma.

Exhibit 28: Glaucoma prevalence by baseline IOP

Baseline IOP (mmHg)	% with Glaucoma	Cumulative %
<= 15	13%	13%
16-18	24%	37%
19-21	22%	59%
22-24	19%	78%
25-29	10%	88%
30-34	9%	97%
>= 35	3%	100%

Source: Company reports

AERI plans to commercialize the drugs itself in the US

AERI estimates that it would need 100 sales reps to target 10,000 high prescribing ophthalmologists in the US. The company intends to partner AR-13324 and PG324 in Europe, Japan and rest of the world. Based on prior history, we believe AERI could be successful in marketing the drugs itself as ophthalmologists will find a new mechanism of treatment attractive and respond to detailing. The message for AR-13324 is likely to be a new mechanism of action, safety and convenience. The message for PG324 is likely to better efficacy than any other drug on the market.

Exhibit 29: AR-13324 and PG324 US revenue build

US Revenue Summary (\$ in MM)	2017E	2018E	2019E	2020E	2021E	2022E	2023E
Annual TRx - 1st Line	17,502,026	17,939,577	18,388,066	18,847,768	19,318,962	19,801,936	20,296,985
% Market Share - PG324	0	89,698	367,761	1,130,866	1,931,896	3,168,310	4,059,397
% Share	0.0%	0.5%	2.0%	6.0%	10.0%	16.0%	20.0%
Annual TRx - 2nd Line	16,198,351	16,603,310	17,018,392	17,443,852	17,879,949	18,326,947	18,785,121
% Market Share - AR-13324	80,992	830,165	1,701,839	2,616,578	2,234,994	1,832,695	1,408,884
% Share	0.5%	5.0%	10.0%	15.0%	12.5%	10.0%	7.5%
Price per Prescription	\$100.00	\$104.00	\$108.16	\$112.49	\$116.99	\$121.67	\$126.53
Gross-to-net Adjustment	20.0%	20.0%	20.0%	20.0%	20.0%	20.0%	20.0%
Total Revenues (\$ MM) - 1st line	0.0	7.5	31.8	101.8	180.8	308.4	410.9
Total Revenues (\$ MM) - 2nd line	6.5	69.1	147.3	235.5	209.2	178.4	142.6
Total Revenues (\$ MM)	6.5	76.5	179.1	337.2	390.0	486.8	553.5

Source: RBC Capital Markets estimates

Exhibit 30: AR-13324 and PG324 EU revenue build

EU Revenue Summary (\$ in MM)	2017E	2018E	2019E	2020E	2021E	2022E	2023E
Annual TRx - 1st Line	28,119,999	28,588,665	29,065,143	29,549,562	30,042,055	30,542,756	31,051,802
% Market Share - PG324	0	0	387,535	1,181,982	2,002,804	3,257,894	4,140,240
% Share	0.0%	0.0%	1.3%	4.0%	6.7%	10.7%	13.3%
Annual TRx - 2nd Line	26,025,421	26,459,178	26,900,165	27,348,501	27,804,309	28,267,714	28,738,843
% Market Share	0	881,973	1,793,344	2,734,850	2,317,026	1,884,514	1,436,942
% Share	0.0%	3.3%	6.7%	10.0%	8.3%	6.7%	5.0%
Price per Prescription	\$100.00	\$100.00	\$100.00	\$100.00	\$100.00	\$100.00	\$100.00
Gross-to-net Adjustment	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
Total Revenues (\$ MM) - 1st line	0.0	0.0	38.8	118.2	200.3	325.8	414.0
Total Revenues (\$ MM) - 2nd line	0.0	88.2	179.3	273.5	231.7	188.5	143.7
Total Revenues (\$ MM)	0.0	88.2	218.1	391.7	432.0	514.2	557.7
1st line Royalties (\$ MM)	0.0	0.0	6.8	20.7	35.0	57.0	72.5
2nd line Royalties (\$ MM)	0.0	15.4	31.4	47.9	40.5	33.0	25.1
Total Royalties (\$MM)	0.0	15.4	38.2	68.5	75.6	90.0	97.6

Source: RBC Capital Markets estimates

Financial projections and model assumptions

AERI's revenues will come from two drugs, AR-13324 and PG324, that are in clinical development at this time. Both are based on a new mechanism of action being developed for the treatment of glaucoma. We expect AR-13324 to get approved and be on the market in 2017 and for PG324 to be on the market in 2018 in the US. We assume these drugs could launch in the EU in 2018 and 2019, respectively. Since AERI's clinical development efforts are focused, these are the only two drugs it is developing, and selling and marketing expenses are also expected to be manageable, we forecast rapid profitability starting in 2018.



Since AERI has worldwide rights to AR-13324 and PG324, it could opt to commercialize the products itself, partner them globally or regionally, or sell the company outright. We currently assume that AERI would market and sell them itself in the US via a proprietary sales force of ~100 sales professionals and partner these compounds outside the US, which is in line with management guidance. A partnership could involve a profit split or co-promote structure or more likely straight royalties on product sales. We assume AERI will receive royalties of 15-20% on AR-13324 and PG324 sales outside the US, primarily in the EU. Sales in additional territories could be upside to our forecasts.

Revenues. We forecast first AR-13324 sales in 2017 and PG324 sales in 2018. We currently expect AR-13324 and PG324 commercialization to be the primary contributors of revenue. We forecast revenues of \$6.5MM in 2017, \$378.4MM in 2020, the third full year of products on the market, and \$612.1MM in 2023. Our estimates could prove conservative especially if PG324 succeeds in showing the overall best safety and efficacy profile of any drug currently available for glaucoma. Upside could also come from revenues related to upfront and milestone payments upon partnering AR-13324 and PG324 outside the US as well as sales in regions beyond the US and EU.

Royalty revenues. We forecast the EU approvals and launch to lag roughly one-year behind US timelines. We forecast a royalty rate of 17.5%, and royalties of \$9.3MM in 2018, \$41.1MM in 2020, and \$58.6MM in 2023. Sales and royalties outside the US and EU would be upside to our current forecasts. We currently assume a partner would take over all manufacturing, marketing, selling and distribution efforts outside the US and pay AERI a flat royalty. However, AERI could also supply drug in return for a transfer price.

COGS and gross margin. Both AERI products are small molecules inhibitors of rho kinase, norepinephrine transporter and protein kinase C. These eye drops are administered as one drop, once per day, alone or in combination with a prostaglandin. We assume a cost of goods sold of ~10% and a gross margin of ~90%, which remains steady over time.

R&D expenses ramp up and go down. We expect R&D expenses to increase from \$16.5MM in 2014 to \$22.5MM in 2016 and then decline thereafter. Our estimates are based both on AERI's guidance in its use of proceeds as well as the focused pipeline, which will invest mostly in AR-13324 and PG-324 development. R&D expenses between fourth quarter 2013 and end of 2015, when AR-13324 pivotal data should be available, total ~\$40MM.

SG&A expenses likely to ramp up starting in 2016. Currently, we model AERI could market AR-13324 and PG324 in the US by itself. Since we forecast AR-13324 approval in 2017, we begin ramping up SG&A in 2016, one year ahead of launch, followed by bigger increases in 2017 and 2018. We estimate SG&A is ~20% of product sales starting 2020 and going forward.

Income tax rate. We forecast a tax rate of 34%. As of December 31, 2012, AERI had net operating loss carryforwards \$60.8MM.

Net income. AERI could be profitable in 2018 depending upon how quickly product sales ramp and whether or not it chooses to invest in the pipeline beyond AR-13324 and PG324. We forecast an EPS of \$0.52 in 2018, which increases to \$4.40 in 2020, the third full year of products on the market, and \$6.80 in 2023.

Shares outstanding. AERI has approximately 23.2MM shares outstanding after the recently closed initial public offering. This total excludes stock options, warrants, restricted stock units, and any other employee stock purchase plans. We currently assume a secondary offering around mid-2015, after AERI has presented Phase IIb data for PG324 in 2016 and



top-line Phase III efficacy data for AR-13324 in 2015. Depending upon whether AERI partners AR-13324 and PG324 outside the US or not and the terms of that partnership could determine how, if any, capital AERI needs before achieving sustained profitability. AERI could also opt for other non-dilutive financing options such as debt or a sales of all or some portion of future royalties outside the US.

Cash and equivalents of ~\$68.4MM from the IPO. AERI completed its US initial public offering (IPO) on October 25, 2013 and exercise of the over-allotment option on October 30 to raise approximately \$68.4MM. The company ended June 2013 with ~\$2.4MM in cash. Therefore, pro forma cash balance after the IPO is roughly \$61.4MM. Based on our current forecasts we assume an additional financing around mid-2015 though we note that AERI has several options available to commercial AR-13324 and PG324 as it owns all rights to all compounds in its pipeline.

Valuation: Base, upside and downside case

Our base, upside and downside case are based on a sum-of-the-parts discounted cash flow (DCF) analysis for AERI's products. We also use a company level DCF and P/E multiple based approach.

- **Sum-of-the-parts DCF (primary valuation approach).** We arrive at our \$20 per share price target using a sum-of-the parts discounted cash flow analysis for AERI shares. The primary components of our valuation include AERI's AR-13324 and PG-324 product sales in the US and royalty revenues from sales in the EU. Our base, upside and downside scenarios use a discount rate of 15% to reflect potential clinical risk and assign a 60% probability of success to AR-13324 and PG324 as AR-13324 must no be evaluated in a longer term study and PG324 must be tested in patients.
- **Company DCF.** A company level DCF supports a similar valuation of \$21 per share.
- **P/E based valuation.** However, valuation using a P/E multiple based methodology supports \$23 per share.

While we believe clinical risk is somewhat high, both regulatory and commercial risk should be low as long as AR-13324 and PG324 demonstrate the level of efficacy and safety expected of them. We believe under such a scenario regulatory authorities and clinicians could look favorably upon the first new mechanism of action to be introduced for the treatment of glaucoma in nearly 20 years.

Potential levers for upside. Upside would come from positive Phase IIb data for PG324 and positive Phase III data for AR-13324. Both could cause us to increase the probability of success assumed, and possibly make adjustments to market share assumptions, especially if PG324 pivotal studies are positive and the drug has a clean safety profile. A partnership with a pharmaceutical or biotechnology company for the development of AR-13324 and PG324 could also lead us to include milestones for clinical, regulatory and commercial success as well as to lower the discount rate as AERI could benefit from the capabilities of a potentially larger partner with greater resources.

Base case: \$20 per share

We value AERI at \$20 per share, which includes US and EU sales of AR-13324 and PG324. We assign a probability of success of 60% to both products and a value of ~\$14 per share to the US and \$6 per share to the EU opportunity. We assume a US launch in 2017 and an EU launch in 2018. Currently, we assume that AERI will sell AR-13324 and PG324 in the US and a



partner will commercialize these compounds outside the US. We forecast peak PG324 sales of \$700-800MM in the US and \$500-600MM in the EU and AR-13324 sales of \$200-300MM in the US and \$100-200MM in the EU. We currently assign no additional value to the earlier stage pipeline. Finally, we assume product sales extend into 2030 and include a terminal value based on a terminal growth rate of -50% and a discount rate of 15%.

Upside case: \$32 per share

Our upside scenario includes ~\$23 per share in value for the US opportunity and ~\$9 per share in value for the EU opportunity. We forecast peak PG324 sales of \$1.2-1.3B in the US and \$900MM-\$1B in the EU and AR-13324 sales of \$200-300MM in the US and \$200-300MM in the EU. We assign products in the pipeline a 60% probability of success, a discount rate of 15%, and use a terminal growth rate of -50%.

Downside case: \$7 per share

Our downside scenario assumes that PG324 will not be approved in the US or EU and AR-13324 will be the primary value driver with most sales coming from the 2nd-line glaucoma treatment market. We value the US opportunity at ~\$5 per share and the EU opportunity at \$3 per share. We assume market share ramps up to roughly 15% of total second-line glaucoma prescriptions in the US and 10% in the EU. Under such a scenario peak sales forecast to be \$400-500MM in the US and \$300-400MM in the EU. We assign AR-13324 a 60% probability of success, a discount rate of 15%, and use a terminal growth rate of -50%.

Exhibit 31: Aerie Pharmaceuticals sum of the parts scenario analysis and valuation summary

Sum of the Parts	Discount Rate	Prob.	US	EU	Total
Base Case	15.0%	60.0%	\$14	\$6	\$20
Upside Case	15.0%	60.0%	\$23	\$9	\$32
Downside Case	15.0%	60.0%	\$5	\$3	\$7
DCF Based	15.0%				\$21
P/E Based	15.0%				\$26

Source: RBC Capital Markets

AERI discounted cash flow analysis

A company level DCF analysis supports a value of ~\$21 per share with the following assumptions: a discount rate of 15%, -50% terminal growth rate, a 34% tax rate, and cash per share of ~\$2. Our revenues include sales of AR-13324 and PG324 in the US and royalties on product sales outside the US. We also assume a growth rate of 5% per year beyond 2023 and an operating margin of 50%.



Exhibit 32: Aerie Pharmaceuticals discounted-cash-flow analysis

Discounted Cash Flow Analysis	
Assumption: Terminal Growth	-50.0%
Assumption: Discount Rate	15.0%
Assumption: Valuation Year	2014
NPV Sum	576.9
Current net cash	68.4
Net cash / share	\$2
Shares outstanding	30.5
Price / Share	\$21

Source: RBC Capital Markets

Aerie Pharmaceuticals P/E multiple based valuation

We use a P/E multiple of 12x our 2021 fully taxed GAAP EPS estimate of \$4.99 and a discount rate of 15% for eight years to arrive at our price target of \$23/share. This P/E multiple could be conservative given that the median P/E for a group of large and profitable biotechnology companies is 22x and 26x, respectively.

Exhibit 33: Aerie Pharmaceuticals P/E multiple based valuation analysis

		PE Multiple						
		9.0	10.0	11.0	12.0	13.0	14.0	15.0
Discount Rate	9.0%	\$24.56	\$27.29	\$30.01	\$32.74	\$35.47	\$38.20	\$40.93
	11.0%	\$21.62	\$24.02	\$26.43	\$28.83	\$31.23	\$33.63	\$36.04
	13.0%	\$19.08	\$21.20	\$23.32	\$25.44	\$27.56	\$29.68	\$31.80
	15.0%	\$16.88	\$18.75	\$20.63	\$22.50	\$24.38	\$26.25	\$28.13
	17.0%	\$14.96	\$16.62	\$18.28	\$19.94	\$21.60	\$23.27	\$24.93
	19.0%	\$13.28	\$14.76	\$16.24	\$17.71	\$19.19	\$20.66	\$22.14
	21.0%	\$11.82	\$13.13	\$14.45	\$15.76	\$17.07	\$18.39	\$19.70

Source: RBC Capital Markets

Price target impediments

Our price target is dependent solely on the clinical, regulatory and commercial success of AR-13324 and PG324. A Phase IIb study for PG324 and a Phase III study for AR-13324 are expected in 2014 and failure to demonstrate efficacy or safety in one or both of these studies would be a significant setback. Furthermore, any setbacks in regulatory approvals in the US or EU, delay in launch, failure to secure a partnership outside the US for AR-13324 and PG324, increased competition or other limitations to the market potential of these products either due to better efficacy and/or safety outcomes or pricing pressure due to the availability of generic drugs for glaucoma, could negatively impact our valuation.

Seasoned management team is a veteran of the ophthalmic space

AERI's CEO, CSO, CMO and COO all have experience developing, marketing and/or selling ophthalmic drugs at various ophthalmology focused companies. Ophthalmology drugs they have developed and/or commercialized include Acular, Alphagan P, Bepreve, Besivance, Bromday, Istalol, Ocuflox, Retisert, Vitrase, Xibrom, and Zylet among others. These also include drugs developed for the treatment of glaucoma.

Vincente Anido, Jr., Ph.D., CEO and Chairman. Dr. Anido has been CEO since July and chairman since April 2013. **Prior experience:** CEO, Ista Pharmaceuticals; General Partner,



Windamere Venture Partners; CEO, CombiChem; President (Americas Region), Allergan; and Marrion Laboratories.

Casey Kopczynski, Ph.D., CSO and Co-Founder. Dr. Kopczynski co-founded Aerie Pharmaceuticals in 2005. **Prior experience:** Managing Partner, Biotech Initiative; VP (Research), Ercole Biotech; Director (Research) and Member of founding scientific staff, Exelixis; and Research Fellow, University of California, Berkeley.

Brian Levy, OD, CMO. Dr. Levy has been CMO since January 2012. He holds an appointment as Clinical Professor, Department of Ophthalmology, University of Rochester School of Medicine. **Prior experience:** CMO, Bausch & Lomb; Clinical Practice, Toronto, Canada; Associate Professor (Dept. of Ophthalmology), California Pacific Medical Center; COO, Danube Pharmaceuticals; and CSO, Nexis Vision.

Thomas Mitro, COO and President. Mr. Mitro has been president and COO since August 2013. **Prior experience:** VP, Sales & Marketing, Omeros; VP, Sales & Marketing, ISTA Pharmaceuticals; and various positions, Allergan.

Richard Rubino, CFO. Mr. Rubino has been CFO since October 2012. **Prior experience:** SVP and CFO, Medco Health Solutions; various positions, International Business Machine and PricewaterhouseCoopers.



Aerie Pharmaceuticals - Income Statement

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FYE December 31

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(in MM; except per share)	2013E	2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E
REVENUES											
AR-13324					6.5	69.1	147.3	235.5	209.2	178.4	142.6
PG324						7.5	31.8	101.8	180.8	308.4	410.9
Product Sales					6.5	76.5	179.1	337.2	390.0	486.8	553.5
Royalties						9.3	22.9	41.1	45.4	54.0	58.6
Other											
Total Revenues					6.5	85.8	202.0	378.4	435.3	540.8	612.1
EXPENSES											
COGS					0.6	7.7	17.9	33.7	39.0	48.7	55.4
R&D	13.0	16.5	20.0	22.5	20.0	10.0	5.0	5.0	5.0	5.0	5.0
SG&A	7.0	7.5	8.5	15.0	30.0	37.5	45.0	67.4	78.0	97.4	110.7
Other											
Total Expenses	19.9	24.0	28.5	37.5	50.6	55.2	67.9	106.2	122.0	151.0	171.1
Operating Income (Expense)	(19.9)	(24.0)	(28.5)	(37.5)	(44.2)	30.6	134.1	272.2	313.3	389.7	441.0
OTHER											
Interest income	0.2	0.4	0.4	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
Interest expense	(0.7)	(0.2)	(0.2)	(0.2)	(0.2)	(0.2)	(0.2)	(0.2)	(0.2)	(0.2)	(0.2)
Other											
Total Other Income (Expense)	(0.5)	0.2	0.2	0.3	0.3	0.3	0.3	0.3	0.3	0.3	0.3
Income before Tax	(20.4)	(23.8)	(28.3)	(37.2)	(43.9)	30.9	134.4	272.5	313.6	390.0	441.3
Taxes						10.5	45.7	92.6	106.6	132.6	150.1
Net income (loss)	(20.4)	(23.8)	(28.3)	(37.2)	(43.9)	20.4	88.7	179.8	207.0	257.4	291.3
EPS, Basic (GAAP)	(\$1.05)	(\$1.01)	(\$1.06)	(\$1.24)	(\$1.44)	\$0.66	\$2.80	\$5.56	\$6.27	\$7.65	\$8.48
EPS, Diluted (GAAP)	(\$0.73)	(\$0.74)	(\$0.81)	(\$0.97)	(\$1.13)	\$0.52	\$2.20	\$4.40	\$4.99	\$6.11	\$6.80
Shares outstanding, Basic	19.4	23.6	26.6	29.9	30.5	31.1	31.7	32.4	33.0	33.7	34.3
Shares outstanding, Diluted	27.9	32.1	35.1	38.4	39.0	39.6	40.2	40.9	41.5	42.2	42.8
Operating Ratios	2013E	2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E
COGS					10.0%	10.0%	10.0%	10.0%	10.0%	10.0%	10.0%
Gross Margin	NA	NA	NA	NA	90.0%	90.0%	90.0%	90.0%	90.0%	90.0%	90.0%
R&D	NA	NA	NA	NA	308.7%	11.7%	2.5%	1.3%	1.1%	0.9%	0.8%
SG&A	NA	NA	NA	NA	463.0%	43.7%	22.3%	17.8%	17.9%	18.0%	18.1%
Operating Margin	NA	NA	NA	NA	-681.7%	35.7%	66.4%	71.9%	72.0%	72.1%	72.1%
Taxes	34.0%	34.0%	34.0%	34.0%	34.0%	34.0%	34.0%	34.0%	34.0%	34.0%	34.0%
Net Margin	NA	NA	NA	NA	-677.1%	23.8%	43.9%	47.5%	47.6%	47.6%	47.6%

Source: Company reports and RBC Capital Markets estimates.

Balance Sheet - Select Items	2013E	2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E
Cash and cash equivalents	61.3	39.2	102.5	65.0	20.8	29.1	88.6	222.7	416.5	648.1	922.3
Prepaid expenses and other current assets	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1
Total current assets	62.5	40.3	107.7	72.6	30.9	53.5	144.3	326.3	535.8	796.3	1,090.2
Property, plant and equipment, net	0.1	0.0	(0.0)	(0.1)	(0.1)	(0.2)	(0.2)	(0.3)	(0.3)	(0.4)	(0.4)
Total assets	62.6	40.4	107.7	72.6	30.8	53.3	144.1	326.1	535.5	795.9	1,089.8
Current Liabilities											
Total current liabilities	11.8	11.8	11.8	12.3	12.8	13.3	13.8	14.3	15.1	16.5	17.5
Total liabilities	4.6	4.6	4.6	4.6	4.6	4.6	4.6	4.6	4.6	4.6	4.6
Share Capital	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Share Premium	68.5	68.5	162.5	162.5	162.5	162.5	162.5	162.5	162.5	162.5	162.5
Accumulated deficit	(83.5)	(105.7)	(132.4)	(168.0)	(210.3)	(188.2)	(98.0)	83.5	292.1	551.1	844.0
Total stockholders' equity	46.2	24.0	91.3	55.7	13.4	35.5	125.7	307.2	515.8	774.8	1,067.7
Total liabilities and stockholders Equity	62.6	40.4	107.7	72.6	30.9	53.4	144.2	326.1	535.5	795.9	1,089.8
Cash Flow Statement - Select Items	2013E	2014E	2015E	2016E	2017E	2018E	2019E	2020E	2021E	2022E	2023E
Net Income (loss)	(20.4)	(23.8)	(28.3)	(37.2)	(43.9)	20.4	88.7	179.8	207.0	257.4	291.3
Depreciation and amortization	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1
Stock based compensation	1.2	1.6	1.6	1.6	1.6	1.6	1.6	1.6	1.6	1.6	1.6
Net cash provided (used) by operating activities	(17.0)	(22.1)	(30.6)	(37.5)	(44.1)	8.4	59.6	134.2	193.8	231.6	274.3
Purchase of property and equipment and intangible assets	(0.1)	(0.1)	(0.1)	(0.1)	(0.1)	(0.1)	(0.1)	(0.1)	(0.1)	(0.1)	(0.1)
Net cash used in investing activities	(0.1)	(0.1)	(0.1)	(0.1)	(0.1)	(0.1)	(0.1)	(0.1)	(0.1)	(0.1)	(0.1)
Proceeds from issuances	68.4		94.0								
Net cash provided by (used in) financing activities	75.4		94.0								
Decrease in cash and cash equivalents	58.4	(22.1)	63.4	(37.5)	(44.2)	8.3	59.5	134.1	193.7	231.6	274.2
Cash and cash equivalents at the beginning of the year	2.9	61.3	39.2	102.5	65.0	20.8	29.1	88.6	222.7	416.5	648.1
Cash and cash equivalents at the end of the year	61.3	39.2	102.5	65.0	20.8	29.1	88.6	222.7	416.5	648.1	922.3

Source: Company reports and RBC Capital Markets estimates.



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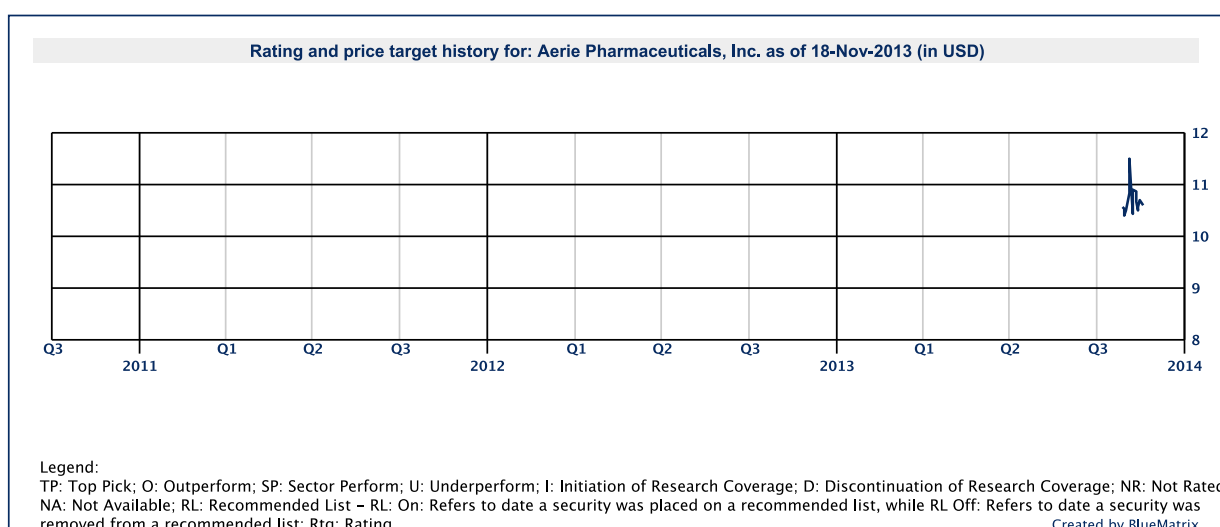
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