Avalanche Biotechnologies (AAVL)

SunTrust Robinson Humphrey

R&D Day: Positive KOL Outlook, Focus on Phase II Data Mid-15 & Pipeline

Buy

Price Target: $60.00
Prior: $60.00

Price (Mar. 24, 2015)	$43.67
52-Wk Range	$60.08-$22.60
Market Cap ($M)	$1,100
ADTV	340,280
Shares Out (M)	25.2
Short Interest Ratio/% Of Float	9.3%
TR to Target	37.4%

Cash Per Share	$8.04
Cash And Equivalents ($M)	$289.9

	2014A	2015E		2016E	
		Curr.	Prior	Curr.	Prior
EPS Adjusted					
1Q	($0.45)	($0.43)	($0.43)	--	
2Q	($2.27)	($0.54)	($0.54)	--	
3Q	($0.50)	($0.66)	($0.66)	--	
4Q	($0.46)	($0.72)	($0.72)	--	
FY	($2.46)	($2.36)	($2.36)	($3.11)	($3.11)
P/E	NM	NM		NM	
Consensus EPS Adjusted					
FY	($2.61)	($1.68)	($1.68)	($1.80)	($1.80)
Revenue ($M)					
FY	$1	$0	$0	$0	$0
P/Sales	1,100.5x	2,392.4x		9,170.7x	
Consensus Rev					
FY	$1	$0	$0	$0	$0

FYE Dec
Quarterly values may not add to the annual value due to rounding.

What's Incremental

AAVL's R&D Day featured 4 key opinion leaders (KOLs) who discussed the outlook of lead gene therapy product AVA-101 for wet AMD. KOLs were positive on: 1) subretinal delivery, 2) impact of prior vitrectomy and 3) risk of atrophy, noting Phase IIa focus on anatomic outcomes and no. of rescue injections. Two new pipeline assets (AVA-322 and AVA-323 for color blindness) were disclosed - with vector readthrough to other diseases. We recommend owning AAVL into the mid-15 AVA-101 data readout (newly-provided baseline characteristics indicative of milder patients vs. Phase I participants).

The key catalyst for AAVL is AVA-101 Phase IIa data readout in mid-15; color on baseline characteristics provides context for expectations. AAVL's lead gene therapy product AVA-101 is currently in an open label Phase IIa study in wet AMD (eye disease where buildup of fluid/blood in the center of the eye results in loss of vision), underway at the Lions Eye Institute (LEI), Australia. The key investor questions relate to readthrough of the impressive Phase I data (+6.3 and +8.7 Best Corrected Visual Acuity (BCVA) letter gain, ~200 microns decrease in retinal thickness) to Phase IIa. We note, the Phase IIa study has targeted “milder" wet AMD patients resulting in a likely more modest clinical improvement with AVA-101. **Newly disclosed at AAVL's R&D Day was color on baseline characteristics for the 32 subjects (N=21 in the AVA-101 arm). Average BCVA and retinal thickness were 63 (35-79) and 332.5 (178-816), respectively, in the Phase II study compared with average 36.5 BCVA (higher value linked to better vision) and 549 (higher value linked to more advanced disease).** 4 Phase IIa patients were treatment-naive and the average duration of disease was 16 months (versus 49 in the Phase I trial). Thus, Phase IIa patients appear indeed milder compared to Phase I participants. In Dr. Jeffrey Heier's (Ophthalmic Consultants of Boston) view, recruitment of milder wet AMD participants reflects increased confidence in this therapy from investigators at the LEI.

KOL expectations for Phase IIa data revolve around anatomic improvement and less on visual change (BCVA). While physicians agree that visual improvement is most important for patients and the approvable endpoint, they believe anatomic changes (retinal thickness decrease, fluid clearance in at least some patients) are most important for AVA-101 activity at this clinical stage. In treatment-experienced patients, KOLs would be happy with maintenance of vision ("would be discouraged to see vision loss"). It is plausible that the 4 treatment-naive patients could experience vision gains, in line with observations with standard of care anti-VEGF injections.

Salveen Richter, CFA
212-319-3728
salveen.richter@suntrust.com

Raluca Pancratov, Ph.D.
212-303-4178
raluca.pancratov@suntrust.com

SEE PAGE 4 FOR REQUIRED DISCLOSURE INFORMATION

KOL feedback was positive on the main AVA-101 controversies brought forward to date as well as on durability. Dr. Szilard Kiss (Cornell Medical College, NYC) provided a positive view on the key 4 concerns we have been discussing with investors. 1) All KOLs agreed that subretinal delivery is a well-established, straightforward surgical procedure, with limited variability among U.S. and int'l eye surgery practices - "top one third procedures in the world in which ophthalmologists are trained". 2) Vitrectomy (a type of surgery available since 1960 to clear out debris/fluid from the eye) is neither beneficial for wet AMD patients (otherwise it would replace widely used anti-VEGF therapy), nor detrimental (3-year follow up data from the Diabetic Clinical Research Network consortium showed no improvement or worsening of BCVA in patients with previous vitrectomy). 3) While the field is still debating the risk of atrophy, it appears to be a natural outcome of wet AMD. An analysis to be presented at ARVO (May 3-7, Denver, CO) will showcase that patients in the CATT trial (N=1024 wet AMD patients given Avastin vs. Lucentis) experienced an inverse correlation between number of injections and presence of atrophy. Another analysis of the CATT study is slated to reveal that no BCVA differences were seen between patients with or without atrophy. 4) If needed, gene therapy could be reversed with a straightforward laser procedure. **Dr. Jean Bennett (UPenn) highlighted the durability of similar AAV-based gene therapies, with persistence and maintained functional benefit of >7 years in humans, >10 years in animals.**

AAVL provided additional details on the early stage pipeline, including the newly announced color blindness program. Avalanche announced today an exclusive in-license agreement with the University of Washington for the development of novel therapies for color blindness. Newly-disclosed in AAVL's pipeline are AVA-322 and AVA-323 for patients with red and green color blindness, respectively. These are two novel genetically engineered AAV-based gene therapy products that emerged from the Ocular Biofactory platform and are amenable to intravitreal delivery. The two investigators at UW that carried out seminal work in this field were present at the R&D Day and discussed the severity of color blindness and its debilitating impact on affected individuals. There are currently no competitive therapies for color blindness (cone photoreceptors play the key role), a ~10M U.S. market. Key investor questions relate to the extent that color blindness is debilitating and/or proportion of patients that would opt for therapy, and whether payors would reimburse such a treatment. Preclinical results to date in non-human primates are suggestive of effective vector delivery to cone cells and functional activity. **Thus, these vectors could have broad utility to other diseases that impact cone photoreceptors (e.g. Stargardt disease, achromatopsia, cone dystrophy, diabetic macular edema, diabetic retinopathy, etc).** Filing of an IND for these products is on track for H2/16. KOLs were most excited about the defined clinical endpoint (gain of color vision), while AAVL noted discussions with the FDA and the agency's positive outlook on its use to design a clinical program. Preclinical work is also advancing for AVA-201, AAVL's next generation wet AMD product suitable for intravitreal delivery (positioned for wet AMD prevention in high risk patients rather than treatment for AVA-101), and AVA-311 for the rare disorder X-Linked Retinoschisis (collaboration with REGN).

AAVL outlined the next steps for AVA-101 and timelines of catalysts. Management discussed the registrational path for AVA-101, noting the well-established roadmap laid out by REGN and RHHBY with the approval of Lucentis and Eylea. Results from this study are expected in mid-15, to inform the design and launch of a Phase IIb trial of AVA-101 for wet AMD in the U.S. A Phase IIb study of AVA-101 is slated to begin in H2/15, to take place mainly in the U.S.: a sham controlled, double blind, dose ranging study of a single subretinal AvA-101 injection. with the primary endpoint of visual acuity evaluated at 52 weeks, with a total 104 weeks of follow up. Sufficient product for this trial has already been manufactured and completed the in-life GMP portion (we spoke with management who appear confident in the comparability of product from the baculovirus manufacturing process vs. prior drug). A large, multi-center Phase III program for AVA-101 in wet AMD will entail study of multiple doses versus the standard of care, and is expected to entail 1 year for enrollment, 1 year for evaluation of the BCVA primary endpoint and 1 year of follow-up. The design may entail non-inferiority or superiority to current anti-VEGF therapies. In parallel, AAVL plans to begin development of AVA-101 for other diseases such as DME or RVO (included in Eylea/ Lucentis' labels). For catalysts, we expect the following: 1) presentation of baseline Phase IIa results at a conference in the spring, potentially as a Late Breaker at ARVO, 2) Phase IIa AVA-101 results in wet AMD in mid-15, 3) potential REGN opt-in for AVA-101, 4) publication of 52-week Phase I AVA-101 data in a scientific journal, 5) launch of a Phase IIb U.S. study of AVA-101 in wet AMD.

SunTrust Robinson Humphrey

Avalanche Biotechnologies

(NASDAQ: AAVL)

Salveen Richter, CFA
(212) 319-3728
salveen.richter@suntrust.com

Consolidated Income Statement

($thousands, except per share data)	FY 2014A	Mar Q1 2015E	Jun Q2 2015E	Sep Q3 2015E	Dec Q4 2015E	FY 2015E	FY 2016E	FY 2017E	FY 2018E	FY 2019E	FY 2020E
Revenue											
AVA-101	$ -	-	-	-	-	$ -	$ -	$ -	$ -	$ -	$ 128,387
% growth (QoQ or YoY)											
AVA-201	$ -					$ -					
% growth (QoQ or YoY)											
AVA-311	$ -					$ -					
% growth (QoQ or YoY)											
Other	$ -					$ -					
% growth (QoQ or YoY)											
Total product revenue						$ -	$ -	$ -	$ -	$ -	$ 128,387
Collaboration and license revenue	572	203	203	203	203	812	812	812	812	812	812
Total Revenue	$ 572	$ 203	$ 203	$ 203	$ 203	$ 812	$ 812	$ 812	$ 812	$ 812	$ 129,199
COGS	-	-	-	-	-	-	-	-	-	-	6,419
Gross profit	572	203	203	203	203	812	812	812	812	812	122,779
Operating expense											
R&D (GAAP)	16,976	7,555	9,978	12,121	13,201	42,855	72,221	98,041	118,334	132,711	143,560
SG&A (GAAP)	7,998	3,401	3,744	4,711	5,102	16,958	25,556	34,210	42,502	65,114	87,001
Total operating expense	24,974	10,956	13,722	16,832	18,303	59,813	97,777	132,251	160,836	197,825	230,561
Operating income (loss)	**(24,402)**	**(10,753)**	**(13,519)**	**(16,629)**	**(18,100)**	**(59,001)**	**(96,965)**	**(131,439)**	**(160,024)**	**(197,013)**	**(107,782)**
Interest Income (expense), net	(6)	16	20	19	18	74	122	169	129	124	116
Other income (expense), net	(70)	-	-	-	-	-	-	-	-	-	-
Change in fair value of warrant liabilities	(722)										
Total Other Income	(1,002)	16	20	19	18	74	122	169	129	124	116
Deemed dividend	(3,230)										
Income before income taxes	(25,404)	(10,737)	(13,499)	(16,610)	(18,082)	(58,927)	(96,843)	(131,270)	(159,895)	(196,889)	(107,666)
Provision for income taxes	-	-	-	-	-	-	-	-	-	-	-
Net gain (loss)	**(28,634)**	**(10,737)**	**(13,499)**	**(16,610)**	**(18,082)**	**(58,927)**	**(96,843)**	**(131,270)**	**(159,895)**	**(196,889)**	**(107,666)**
FX translation adjustment											
Net gain (loss) applicable to common shareholders	$ (28,634)	$ (10,737)	$ (13,499)	$ (16,610)	$ (18,082)	$ (58,927)	$ (96,843)	$ (131,270)	$ (159,895)	$ (196,889)	$ (107,666)
GAAP EPS (diluted)	$ (2.46)	$ (0.43)	$ (0.54)	$ (0.66)	$ (0.72)	$ (2.36)	$ (3.11)	$ (4.18)	$ (4.85)	$ (5.30)	$ (2.76)
Weighted shares outstanding basic and diluted (k)	11,651	24,779	24,902	25,027	25,152	24,965	31,118	31,429	33,000	37,151	39,008
Cash, cash equivalents and marketable securities		$ 279,151	$ 265,632	$ 249,003	$ 230,903		$ 533,938	$ 402,499	$ 242,475	$ 295,462	$ 187,680
Margin Analysis:											
Cost of product sales	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	5%	5%
Product gross margin	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	95%	95%
R&D (GAAP)	2968%	3722%	4915%	5971%	6503%	5278%	8894%	12074%	14573%	16344%	111%
SG&A (GAAP)	1398%	1675%	1844%	2321%	2513%	2088%	3147%	4213%	5234%	8019%	67%
Stock-based compensation expense	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
Total operating expense	4366%	5397%	6760%	8292%	9016%	7366%	12042%	16287%	19807%	24363%	178%
Operating margin	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	-19707%	-24263%	-83%
Income tax provision	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%	0%
Net margin (GAAP)	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	-19692%	-24247%	-83%
Y/Y change:											
Total revenue	119%	677%	150%	100%	100%	142%	100%	100%	100%	100%	15911%
AVA-101 revenue	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
R&D (GAAP)	689%	730%	222%	111%	83%	152%	69%	36%	21%	12%	8%
SG&A (GAAP)	349%	368%	151%	96%	51%	112%	51%	34%	24%	53%	34%
Stock-based compensation expense	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A
Total operating expense	535%	570%	199%	107%	73%	140%	63%	35%	22%	23%	17%
Operating income	606%	570%	204%	109%	74%	142%	64%	36%	22%	23%	-45%
Net income (GAAP)	440%	546%	62%	101%	74%	106%	64%	36%	22%	23%	-45%
GAAP EPS (diluted)	70%	-4%	-76%	32%	56%	4%	-32%	-34%	-16%	-9%	48%
Shares outstanding - GAAP	217%	575%	578%	53%	11%	114%	25%	1%	5%	13%	5%

Source: STRH Research, Company Reports

Company Description

Avalanche Biotechnologies, Inc. is a clinical-stage biotechnology company that develops novel gene therapies to treat patients with sight-threatening ophthalmic diseases. Its products are used for the treatment of wet age-related macular degeneration and Juvenile X-linked Retinoschisis by inducing a sustained expression of a therapeutic protein with a one-time administration in the eye. The company was founded by Mark S. Blumenkranz, Thomas W. Chalberg and Steven D. Schwartz on July 17, 2006 and is headquartered in Menlo Park, CA.

Investment Thesis

Avalanche is one of the slew of new entrants in the biotech space, focused on gene therapy. Broad investor interest in the renaissance of gene therapy is evidenced by the strong performance of most of these stocks over their S1 price. Furthermore, AAVL shares are currently down off its highs at the end of December, providing an entry point ahead of readout of the Phase IIa study of lead product AVA-101 for wet age-related macular degeneration (AMD) in mid-2015. This product consists of an adeno-associated vector-based gene therapy, with the potential to disrupt and expand the $6B+ anti-VEGF market. Clinical results generated to date are suggestive of activity in a small number of patients with advanced disease. A randomized Phase IIa single center study is ongoing in Australia, with results expected, as noted, mid-2015. Given AVA-101's mechanism of action similar to anti-vascular endothelial growth factor (VEGF) biologics Lucentis and Eylea, the product could also have utility beyond wet AMD, in diseases such as retinal vein occlusion or diabetic macular edema (where Lucentis and Eylea are the standard of care). A follow-on preclinical gene therapy product AVA-201 is expected to undergo IND-enabling studies in 2015 for the prevention of high risk wet AMD. Avalanche is collaborating with Regeneron for the development of novel gene therapies for eye diseases, with the first product (preclinical stages) AVA-311 to address the orphan disease X-linked retinoschisis (XLRS). Notably, Regeneron also retains a time-limited right to first negotiation of rights to AVA-101.

Valuation and Risks

Valuation

We arrive at our price target of $60 by means of a sum-of-the-parts discounted cash flow analysis, which ascribes $46.24/share to AVA-101 U.S. sales, $6.11 to AVA-101 E.U. sales, and $8.04/share to cash. We assign AVA-101 in a probability of success of 55% in the U.S. and 25% in the E.U. We assume a discount rate of 12% and a 1% terminal growth rate. We do not model for any additional indications for AVA-101 beyond wet AMD. We do not include any value for AVA-201, AVA-311, or any other follow on products in our valuation.

Investment risks

The primary investment risks for Avalanche include the following:

• **Clinical and safety risk**: Phase I results presented to date showcased some intriguing signs of activity for Avalanche's AVA-101. The limitations of these data, however, include the small number of patients, a single center whereby doctors were well familiar with subretinal injection, and participants with advanced wet AMD who experienced tremendous increases in best corrected visual acuity. There remains the risk that Phase IIa and Phase IIb data do not recapitulate earlier findings due to differences in patient baseline characteristics, variability in time of assessment and determination of whether an anti-VEGF injection is needed, variability in efficacy measurements. There also remains a risk (albeit minimal) that in vivo dosing of AVA-101 could lead to an exaggerated immune reaction, resulting in loss of anti-VEGF molecule expression of significant loss of eye tissue.
• **Regulatory risk:** No gene therapy product has been approved in the U.S. to date, and in spite of the FDA's guidance there remain questions about the appropriate study design for pivotal gene therapy trials, especially for orphan diseases. The agency may require additional information on manufacturing methodology, as well as facilities where all the moving parts of a complex therapy are generated.
• **Commercial risk:** Given the novelty of gene therapy, there remains a risk that physicians are reluctant to prescribe AVA-101 to their patients. We note the risk of AVA-101 not reaching our sales estimates due to potential pricing and reimbursement issues, lower than expected penetration, or lack of ability to effectively target the broad wet AMD market.

• **Competitive Risk:** AVA-101 is entering the established wet AMD market, where two branded products (RHHBY's Lucentis and REGN's Eylea) and off-label Avastin are competing for share of the prevalent patient pool. Furthermore, AVA-101 competes with products such as Ophthotech's Fovista and Allergan's DARPins, which offer alternatives to the current anti-VEGF standard of care. Beyond monthly or every other month injections, AVA-101 is also competing with other gene therapies, including Sanofi/Genzyme's rAAV2-sFLT01, which has also completed Phase I testing. There is a risk that AVA-101 would not capture significant share of the wet AMD market, or of the retinal vein occlusion or diabetic macular edema markets.
• **Financial and partnership risk:** Avalanche does not currently recognize any revenue related to product sales. Given the expenses associated with clinical drug development, we forecast that the company could issue additional equity to finance its activities. There remains a risk that the company's cash reserves may be significantly depleted while attempting to fulfill collaborative obligations for partner Regeneron. There is a risk that no appropriate candidates emerge from the collaboration with Regeneron, thereby jeopardizing the non-dilutive cash inflow associated with this partnership (we do not model for any revenue associated with the partnership apart from the $6.5M upfront payment).

Companies Mentioned in This Note

Avalanche Biotechnologies (AAVL, $43.67, Buy)
Regeneron Pharmaceuticals, Inc. (REGN $453 NR)
Roche Holding Ltd Sponsored ADR (RHHBY $34.85 NR)

Analyst Certification

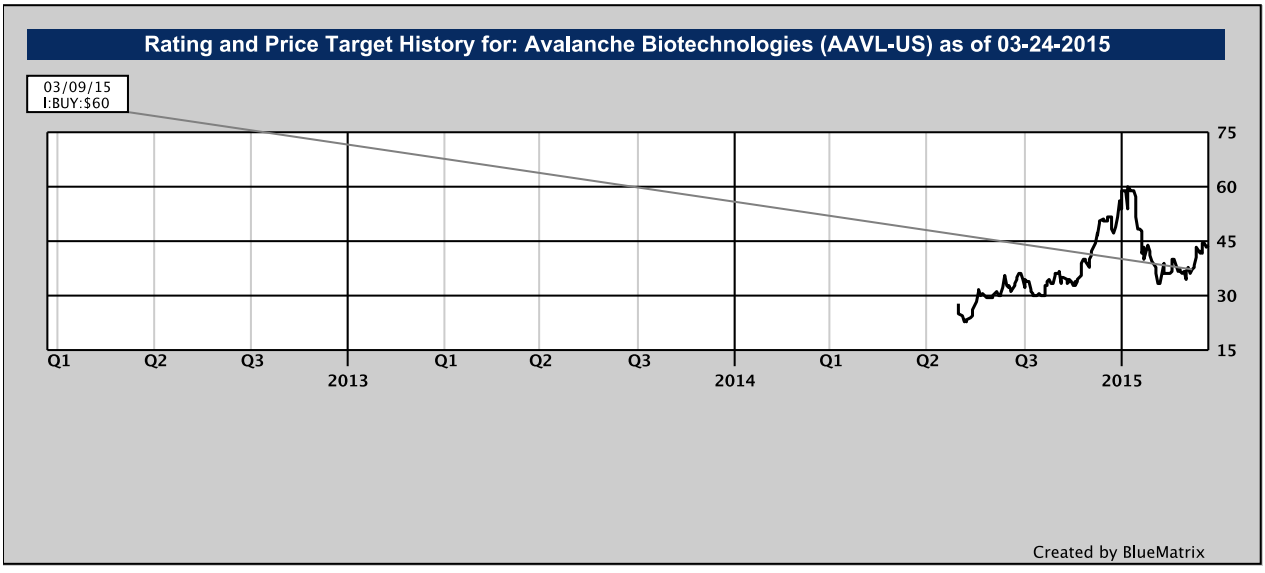
I, Salveen Richter , hereby certify that the views expressed in this research report accurately reflect my personal views about the subject company(ies) and its (their) securities. I also certify that I have not been, am not, and will not be receiving direct or indirect compensation in exchange for expressing the specific recommendation(s) in this report.

Required Disclosures

SunTrust Robinson Humphrey, Inc. makes a market in the following companies at the time of this report: AAVL, AAVL-US

Analyst compensation is based upon stock price performance, quality of analysis, communication skills, and the overall revenue and profitability of the firm, including investment banking revenue.

As a matter of policy and practice, the firm prohibits the offering of favorable research, a specific research rating or a specific target price as consideration or inducement for the receipt of business or compensation. In addition, associated persons preparing research reports are prohibited from owning securities in the subject companies.



STRH Ratings System for Equity Securities

3 designations based on total returns* within a 12-month period**

- **Buy** – total return ≥ 15% (10% for low-Beta securities)***
- **Reduce** – total return ≤ negative 10% (5% for low Beta securities)
- **Neutral** – total return is within the bounds above
- **NR** – NOT RATED, STRH does not provide equity research coverage
- **CS** – Coverage Suspended

*Total return (price appreciation + dividends)
**Price targets are within a 12-month period, unless otherwise noted
***Low Beta defined as securities with an average Beta of 0.8 or less, using Bloomberg's 5-year average Beta

Legend for Rating and Price Target History Charts:
D = drop coverage
I = initiate coverage
T = transfer coverage

SunTrust Robinson Humphrey ratings distribution (as of 03/25/2015):

Coverage Universe			Investment Banking Clients Past 12 Months		
Rating	**Count**	**Percent**	**Rating**	**Count**	**Percent**
Buy	280	52.53%	Buy	101	36.07%
Neutral	242	45.40%	Neutral	45	18.60%
Sell/Reduce	11	2.06%	Sell/Reduce	2	18.18%

Other Disclosures

Information contained herein has been derived from sources believed to be reliable but is not guaranteed as to accuracy and does not purport to be a complete analysis of the security, company or industry involved. This report is not to be construed as an offer to sell or a solicitation of an offer to buy any security. SunTrust Robinson Humphrey, Inc. and/or its officers or employees may have positions in any securities, options, rights or warrants. The firm and/or associated persons may sell to or buy from customers on a principal basis. Investors may be prohibited in certain states from purchasing some over-the-counter securities mentioned herein. Opinions expressed are subject to change without notice. The information herein is for persons residing in the United States only and is not intended for any person in any other jurisdiction.

SunTrust Robinson Humphrey, Inc.'s research is provided to and intended for use by Institutional Accounts as defined in FINRA Rule 4512(c). The term "Institutional Account" shall mean the account of: (1) a bank, savings and loan association, insurance company or registered investment company; (2) an investment adviser registered either with the SEC under Section 203 of the Investment Advisers Act or with a state securities commission (or any agency or office performing like functions); or (3) any other person (whether a natural person, corporation, partnership, trust or otherwise) with total assets of at least $50 million.

SunTrust Robinson Humphrey, Inc. is a registered broker-dealer and a member of FINRA and SIPC. It is a service mark of SunTrust Banks, Inc. SunTrust Robinson Humphrey, Inc. is owned by SunTrust Banks, Inc. ("SunTrust") and affiliated with SunTrust Investment Services, Inc. Despite this affiliation, securities recommended, offered, sold by, or held at SunTrust Robinson Humphrey, Inc. and at SunTrust Investment Services, Inc. (i) are not insured by the Federal Deposit Insurance Corporation; (ii) are not deposits or other obligations of any insured depository institution (including SunTrust Bank); and (iii) are subject to investment risks, including the possible loss of the principal amount invested. SunTrust Bank may have a lending relationship with companies mentioned herein.

ADDITIONAL INFORMATION IS AVAILABLE at our website, **www.suntrustrh.com,** or by writing to: SunTrust Robinson Humphrey, Research Department, 3333 Peachtree Road N.E., Atlanta, GA 30326-1070