Avalanche Biotechnologies, Inc. Announces Positive Top-Line Phase 2a Results for AVA-101 in Wet Age-Related Macular Degeneration

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MENLO PARK, CA -- (Marketwired) -- 06/15/15 --

- Phase 2a study met primary endpoint while demonstrating promising treatment effect on visual acuity maintenance with less frequent injections

- Phase 1 36-month follow-up data demonstrates continued safety and tolerability; rescue injections averaged less than one per year

- Conference call and webcast today at 5:00 p.m. ET

Avalanche Biotechnologies, Inc. (NASDAQ: AAVL) today announced that its Phase 2a clinical study for AVA-101 met its 12-month primary endpoint, based on ophthalmic and systemic safety, demonstrating that AVA-101 was well tolerated with a favorable safety profile in subjects with wet age-related macular degeneration (wet AMD). AVA-101 also showed an improvement on best corrected visual acuity (BCVA) compared with the control group and a positive trend in response rate (stable vision with few rescue injections). AVA-101 is being developed as a sub-retinal gene therapy injection to provide a safe and effective treatment for wet AMD that is durable and reduces the need for frequent anti-VEGF injections.

"The results of this study confirm the Phase 1 safety results and suggest that AVA-101 could potentially benefit a significant portion of patients with wet AMD who require regular treatment with anti-VEGF therapy," said Samuel B. Barone, M.D., Avalanche's chief medical officer. "The current standard of care in wet AMD requires frequent anti-VEGF injections, which present a significant burden for patients and their caregivers, and can result in reduced treatment compliance and under-treatment. Therefore, a product that can maintain or improve vision while reducing the number of treatment injections would represent a powerful new option for patients and physicians."

In the study, BCVA mean change from baseline showed a difference of 11.5 letters between the treatment (+2.2 letters) and control (-9.3 letters) groups (95 percent CI, 2.3-20.7 letters). Additionally, a significant number of AVA-101 treated subjects (42.9 percent) improved or maintained stable vision with two or fewer rescue injections compared with subjects in the control group (9.1 percent). Importantly, BCVA improvement of at least 10 letters with two or fewer rescue injections was observed in 23.8 percent of treated subjects and 0 percent of subjects in the control group.

"AVA-101 demonstrated tolerability and a promising treatment effect in the subjects treated in this study, many of whom had been extensively treated with anti-VEGF therapy prior to enrollment and showed difficult-to-treat characteristics including persistent recurrent wet AMD activity," said Thomas W. Chalberg, Jr., Ph.D., Avalanche's co-founder and chief executive officer. "These data will help inform our future study designs, including the Phase 2b study that we plan to initiate later this year. We believe AVA-101 has the potential to substantially improve the standard of care and lower the high burden of treatment for patients suffering from wet AMD."

The Phase 2a study enrolled 32 subjects age 55 or older with wet AMD and randomized them to an AVA-101 treatment group (n=21) or a control group (n=11). Subjects in both groups received two ranibizumab injections at day 0 and week 4, and ranibizumab rescue therapy was allowed according to pre-specified criteria beginning at week 8. Twenty-nine of 32 subjects had received prior anti-VEGF therapy, with a median of 10 prior injections.[(1)] The primary endpoint of the study was safety, as measured by ophthalmic and/or systemic complications. Secondary endpoints included mean change from baseline in BCVA, the number of ranibizumab rescue injections, and mean change from baseline in central retinal thickness as measured by SD-OCT. All subjects remained in the study through the 12-month study visit.

No serious adverse events related to AVA-101 were observed. One subject in the treatment group experienced a non-fatal myocardial infarction classified as unrelated to therapy. In the control group, one case of endophthalmitis was observed. All adverse events related to study drug were mild or moderate and resolved within 60 days. There were no unexpected administration-related adverse events, and any events that occurred resolved without visual sequelae.

Although the study was not designed to show statistically significant differences between the active and control subjects in the secondary endpoints, the following results were observed:

- Overall, BCVA mean change from baseline did show a significant difference of 11.5 letters between the treatment (+2.2 letters) and control (-9.3 letters) groups (95 percent CI, 2.3-20.7 letters).
- More AVA-101 treated subjects improved or maintained stable vision (>-5 letters) with a low number (≤2) of rescue treatments. Specifically, 23.8 percent (treated) vs. 9.1 percent (control) maintained stable vision with ≤1 rescue injections, and a significant number of AVA-101 treated subjects (42.9 percent) improved or maintained stable vision with ≤2 rescue injections compared with subjects in the control group (9.1 percent).
- BCVA improvement of ≥10 letters with ≤2 rescue injections was observed in 23.8 percent of treated subjects and 0 percent of subjects in the control group.
- The median number of rescue injections using the protocol-specified retreatment regimen was 2 (95 percent CI, 1-6 injections) in AVA-101 treated subjects compared with 4 (95 percent CI, 3-5 injections) in the control group. More subjects

required fewer retreatments in the treatment group compared with control (19.0 percent vs. 9.1 percent with 0 injections; 33.3 percent vs. 9.1 percent with ≤1 injections; 52.4 percent vs. 9.1 percent with ≤2 injections).
- Retinal thickness mean change from baseline, as reported by the site using automated segmentation, was +25 mm for AVA-101 treated subjects compared with -56 mm in the control group (CI for the difference, 17 to 145 mm). Additional evaluation of SD-OCT images by an image reading center are ongoing.

Detailed data from the AVA-101 Phase 2a study will be presented at upcoming medical conferences this year. These data will help inform the design of Avalanche's Phase 2b AVA-101 study, which the Company plans to conduct at multiple centers in the United States.

Phase 1 Study 36-Month Data
Avalanche also announced today 36-month follow up data on eight subjects treated in the Phase 1 study of AVA-101, which confirmed the safety profile of the drug previously reported at 12 months. Long-term follow-up for subjects from the Phase 1 study included planned visits at 18 and 36 months to evaluate long-term safety. During the long-term follow up period, anti-VEGF rescue treatment was determined at the discretion of the subject's physician. Six of the eight subjects were available for evaluation at 36 months, four from the treatment group and two from the control group. Two subjects withdrew from the study for reasons unrelated to study drug. Through 36 months, AVA-101 was shown to be well tolerated with no significant drug-related safety concerns in all four subjects from the treatment group. Among the four AVA-101 treated subjects with data available through 36 months, the mean change from baseline to month 36 was +0.5 letters and subjects received an average of 0.71 rescue injections per year, after the two required ranibizumab injections. Detailed data from this long-term follow up study will be reported at a medical meeting later this year.

Conference Call Today at 5:00 p.m. Eastern Time (2:00 p.m. Pacific Time)
Avalanche will host a teleconference and webcast to discuss the information in this press release. The live call may be accessed by phone by calling (844) 824-7426 (domestic) or (330) 863-3278 (international), conference ID 62079488. The webcast can be accessed on the Investor Relations section of the Avalanche website at www.avalanchebiotech.com and will be archived for 14 days following the call. A replay of the call will be available by phone by calling (855) 859-2056, participant code 62079488.

About AVA-101
AVA-101 gene therapy is being developed as a single sub-retinal injection to provide a safe and effective treatment for wet AMD that is durable and reduces the need for frequent injections. AVA-101 is comprised of the AAV2 vector, which contains a gene encoding sFlt-1, a naturally-occurring anti-VEGF protein. When administered in the eye and expressed by the host retinal cells, the sFlt-1 protein inhibits the formation of new blood vessels and reduces vascular permeability by binding and blocking VEGF activity.

About Wet AMD
Age-related macular degeneration (AMD) is a progressive disease affecting the retinal cells in the macula, the region of the eye responsible for central vision. Wet AMD is an advanced form of AMD where blood vessels begin to invade the cellular space between layers of cells in the retina. These new blood vessels are often leaky, which results in fluid and blood in the retina and causes vision loss. While wet AMD represents only 10 percent of the number of cases of AMD overall, it is responsible for 90 percent of AMD-related severe vision loss. Of untreated patients who are not already partially sighted or blind, over half will become partially sighted or blind within three years. Each year, approximately 150,000 Americans develop wet AMD, with the number expected to grow due to the aging U.S. population.

About Avalanche Biotechnologies, Inc.
Avalanche is a biopharmaceutical company committed to improving or preserving the sight of people suffering from blinding eye diseases with an unmet medical need. Avalanche's proprietary Ocular BioFactory™ is a platform for discovering and developing novel medicines with the potential to offer life-changing therapeutic benefit. Avalanche's lead product candidate, AVA-101, is in mid-stage clinical development for patients with wet age-related macular degeneration. For more information, please visit ***www.avalanchebiotech.com***.

Forward-Looking Statements
Except for the historical information contained herein, the matters set forth in this press release, including statements regarding Avalanche's plans, potential opportunities, expectations, projections, goals, objectives, milestones, strategies, product pipeline, clinical studies, product development and the potential benefits of its products under development, are forward-looking statements within the meaning of the "safe harbor" provisions of the Private Securities Litigation Reform Act of 1995. Such forward-looking statements involve substantial risks and uncertainties that could cause our product development program, clinical development programs, future results, performance or achievements to differ significantly from those expressed or implied by the forward-looking statements. Such risks and uncertainties include, among others, the uncertainties inherent in the clinical development process, including the risk that positive results from a clinical study of AVA-101 may not necessarily be predictive of the results of future clinical studies, the uncertainties inherent in the regulatory approval process, the timing of our regulatory filings and other matters that could affect the availability or commercial potential of our product candidates. Avalanche undertakes no obligation to update or revise any forward-looking statements. For a further description of the risks and uncertainties relating to the business of Avalanche, see our Annual Report on Form 10-K for the year ended December 31, 2014, filed with the Securities and Exchange Commission on March 5, 2015, and our subsequent periodic reports filed with the Securities and Exchange Commission.

(1) Rakoczy, E.P (2015 May) *Baseline Data for Patients Participating in the Phase 2a rAAV.sFLT-1 Gene Therapy Trial for Exudative AMD* Poster session presented at American Society of Gene and Cell Therapy, New Orleans, LA.

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