Aerpio Pharmaceuticals Presents Data Showing Potential of AKB-9778, a VE-PTP Inhibitor/Tie2 Activator, to Lower Intra-ocular Pressure in Human Subjects

May 2, 2019

Data presented during "The Role of the Tie2 Pathway in Ocular Disease" symposium at the Association for Research in Vision and Ophthalmology (ARVO) 2019 Annual Meeting

CINCINNATI--(BUSINESS WIRE)--May 2, 2019-- Aerpio Pharmaceuticals, Inc. (NASDAQ: ARPO), a biopharmaceutical company focused on developing compounds that activate Tie2 to treat ocular diseases and diabetic complications, presented data showing the potential of AKB-9778, a VE-PTP inhibitor and Tie2 activator, to lower intra-ocular pressure (IOP) in human subjects. The data were presented as part of Special Session, entitled "The Role of the Tie2 Pathway in Ocular Disease," at The Association for Research in Vision and Ophthalmology (ARVO) 2019 Annual Meeting on May 1 in Vancouver, British Columbia.

The data on IOP were collected from two Phase 2 clinical trials, TIME-2 and TIME-2b, that were designed to evaluate the safety and efficacy of subcutaneous AKB-9778 in patients with diabetic macular edema (TIME-2) and non-proliferative diabetic retinopathy (TIME-2b). In both studies, measurements of IOP were prospectively included as safety outcomes in the study protocols.

Data from the TIME-2 clinical trial (presented at ARVO 2018, Abstract no. 1252) showed that twice-daily, subcutaneous administration of 15 mg twice daily of AKB-9778 significantly reduced IOP in these ocular normotensive patients by -1.20 ± 0.21 mmHg compared to -0.17 ± 0.30 mmHg in patients receiving placebo (mean change from baseline ± SE; $p < 0.01$).

These results were confirmed in the TIME-2b clinical trial and were observed from the first visit on week 12 through the last visit on week 48 (Fig. 2). Similar to TIME-2, AKB-9778 15 mg twice daily significantly reduced IOP by -1.10±0.23 mmHg compared to +0.15±0.23 in placebo patients (mean change from baseline ± SE; $p < 0.001$).

Figure 2. Effects on IOP (mmHg) at different timepoints from TIME-2b (mean change from baseline ± SE)

	Week 12	Week 24	Week 36	Week 48
Placebo (n=57)	+0.45±0.40	+0.50±0.39	+0.62±0.52	+0.34±0.35
AKB-9778 QD (n=55)	-0.56±0.38	-0.56±0.40	-0.94±0.46	-0.72±0.38
AKB-9778 BID (n=55)	-0.91±0.43	-1.27±0.45	-1.48±0.47	-0.94±0.40

"Although the TIME-2 and TIME-2b studies were designed to evaluate conditions other than glaucoma and included subcutaneous administration rather than a topical ocular formulation, which is typically used for this disease, we were encouraged by the consistent IOP reductions observed in two different studies," said Stephen Hoffman, M.D., Chief Executive Officer of Aerpio. "In addition, these results are consistent with what we observed in preclinical studies in animal models, including a study presented at this conference on April 29. We are looking forward to initiating clinical development of a topical ocular formulation of AKB-9778 in the second quarter of 2019."

Janey Wiggs, M.D., Ph.D., Associate Chief, Ophthalmology Clinical Research; Associate Director, Howe Laboratory, Massachusetts Eye and Ear Infirmary added, "The genomic work that I presented at this symposium suggests a role for the Tie-2 pathway in the control of IOP through the conventional outflow pathway. The clinical effects of Tie-2 activation on IOP that were presented by Dr. Peters are consistent with the genomic work. These data suggest that Tie2 activation is a promising approach for the treatment of glaucoma."

Dr. Wiggs reports receiving consulting fees from Aerpio Pharmaceuticals.

Presentation details:

Presentation Title: Schlemm's canal, a critical outflow channel for the eye, is made up of hybrid vascular/lymphatic endothelial cells. Activation of Tie2 by inhibition of VE-PTP stimulates aqueous outflow and lowers IOP.
Session Title: The Role of the Tie2 Pathway in Ocular Disease
Session Date and Time: Wednesday, May 1, 2019 from 6:15 p.m. – 7:45 p.m. PDT
Presentation Date and Time: Wednesday, May 1, 2019 from 7:30 p.m. – 7:45 p.m. PDT
Presenter: Kevin G. Peters, M.D., Chief Scientific Officer, Aerpio Pharmaceuticals
Location: Vancouver Convention Center Room West 109/110

Abstracts and full session details can be found at www.arvo.org.

About Aerpio Pharmaceuticals

Aerpio Pharmaceuticals, Inc. is a biopharmaceutical company focused on advancing first-in-class compounds that activate Tie2 to treat ocular diseases and complications of diabetes. Tie2 is an important regulator of vascular stability and its down-regulation is found in patients with diabetes and other conditions. Down-regulation is caused by activation of two inhibitors of Tie2, VE-PTP and Ang-2. The Company's lead compound, AKB-9778, is being investigated for its potential utility in treating diabetic nephropathy and an eyedrop formulation is in development as a potential

treatment for open-angle glaucoma. For more information, please visit www.aerpio.com.

About the TIME-2 Study

The TIME-2 study evaluated 144 diabetic macular edema (DME) patients randomized equally (1:1:1) to AKB-9778 as monotherapy or in combination with Lucentis® compared with Lucentis® alone for a treatment period of 3 months, followed by a 2-month observation period. The study's primary endpoint measure was mean change from baseline in CST at 3 months. Pre-specified analyses of change in diabetic retinopathy severity score were done by treatment group in the study eye. Evaluation of the fellow eye was done by combining groups that received subcutaneous AKB-9778, AKB-9778 monotherapy and AKB-9778 + Lucentis® combination therapy groups and comparing changes in diabetic retinopathy severity score in patients that received subcutaneous placebo (ranibizumab monotherapy group).

About the TIME-2b Study

The TIME-2b study was a double-masked, placebo-controlled, multi-center trial that enrolled 167 patients randomized to receive 48-weeks of treatment with either AKB-9778 15 mg subcutaneously once daily, AKB-9778 15 mg subcutaneously twice daily, or placebo subcutaneously twice daily. The primary endpoint of the TIME-2b study is the percentage of patients who improve by 2 or more steps in diabetic retinopathy severity score (DRSS) in the study eye. Secondary objectives include assessment of DRSS improvement in the fellow eye in patients with bilateral disease, proportion of patients that develop diabetic macular edema and/or proliferative diabetic retinopathy, and improvement in renal function. More information about the clinical trial is available at: https://clinicaltrials.gov/ct2/show/NCT03197870.

Forward-Looking Statements

This press release contains forward-looking statements. Statements in this press release that are not purely historical are forward-looking statements. Such forward-looking statements include, among other things, the development of the Company's product candidates, including AKB-9778, the Company's plans for future development of its product candidates, including the timing and commencement of the Company's planned clinical trials, the role of VE-PTP and the Tie2 pathway in treatment of diabetic complications, including ocular hypertension in glaucoma, and the therapeutic potential of the Company's product candidates. Actual results could differ from those projected in any forward-looking statements due to several risk factors. Such factors include, among others, the ability to continue to develop AKB-9778 or other product candidates, the inherent uncertainties associated with the drug development process, including uncertainties in regulatory interactions, commencing clinical trials and enrollment of patients in clinical trials, competition in the industry in which the Company operates and overall market conditions.

These forward-looking statements are made as of the date of this press release, and the Company assumes no obligation to update the forward-looking statements, or to update the reasons why actual results could differ from those projected in the forward-looking statements, except as required by law. Investors should consult all the information set forth herein and should also refer to the risk factor disclosure set forth in the reports and other documents the Company files with the SEC available at www.sec.gov.

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