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Chugai In-Licenses RNAi Therapeutic Zilebesiran for Hypertension with High Cardiovascular Risk

- Chugai obtained commercialization rights in Japan for zilebesiran, an investigational RNAi therapeutic for hypertension with high cardiovascular risk, from Roche
- Since hypertension is the leading cause of cardiovascular disease and uncontrolled hypertension can lead to cerebrovascular and cardiovascular diseases, there remains a significant unmet medical need

TOKYO, April 19, 2024 – Chugai Pharmaceutical Co., Ltd. (TOKYO: 4519) announced that it concluded a license agreement with Roche (SIX: RO, ROG; OTCQX: RHHBY) for zilebesiran, an investigational RNAi therapeutic for hypertension created by Alnylam Pharmaceuticals, Inc. (NASDAQ: ALNY) and currently under development by Roche and Alnylam. Under the license agreement between Roche and Chugai, Chugai obtained commercialization rights in Japan for zilebesiran. Roche will receive an upfront fee and milestone payments.

"Hypertension is a serious disease that can lead to the onset and recurrence of various cerebrovascular and cardiovascular events including myocardial infarction and stroke. However, up to 80%[1] of patients with hypertension still show uncontrolled blood pressure and there remains a significant unmet need. Chugai will work closely with Roche and Alnylam to bring innovations through this new modality to patients with hypertension as soon as possible," said Chugai's President and CEO, Dr. Osamu Okuda.

Zilebesiran is an RNAi therapeutic targeting angiotensinogen (AGT) that reduces vasoconstrictor angiotensin II by inhibiting the synthesis of angiotensinogen in the liver. Alnylam conducted the global Phase II KARDIA-2 study of zilebesiran in patients with mild to moderate uncontrolled hypertension evaluating the efficacy and safety of a single subcutaneous dose of zilebesiran when added to one of three standard of care antihypertensives. The primary endpoint was the change from baseline mean systolic blood pressure (SBP) at month three, assessed by 24-hour ambulatory blood pressure monitoring (ABPM). The KARDIA-2 study met its primary endpoint, demonstrating clinically and statistically significant additive, placebo-adjusted SBP reductions. The global Phase II KARDIA-3 study was recently initiated in patients at high cardiovascular risk and uncontrolled hypertension to evaluate the efficacy of zilebesiran when added to two or more hypertensive medications.

Chugai will continue to effectively utilize the research and development resources of the Roche Group to find innovative new drugs so as to satisfy unmet medical needs.

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About hypertension

Hypertension is the leading cause of cardiovascular disease worldwide, and a major risk for premature mortality.[1] Early effects of hypertension can include subtle target organ damage such as left-ventricular hypertrophy and cognitive dysfunction.[2,3] Over time, uncontrolled hypertension can lead to cardiovascular disease including stroke (ischaemic and haemorrhagic), coronary artery disease, heart failure, peripheral artery disease, chronic kidney disease and end-stage renal disease, dementia, and Alzheimer's disease.[4,5,6,7] There remains a significant unmet medical need, as poor rates of adherence to daily medications can result in inconsistent blood pressure control and an increased risk for stroke, heart attack, and premature death.[8] In particular, there are a number of high unmet need settings where novel approaches to hypertension warrant additional development focus, including patients at high cardiovascular risk.[9]

About zilebesiran

Zilebesiran is an investigational, subcutaneously administered RNAi therapeutic targeting angiotensinogen (AGT) in development for the treatment of hypertension in high unmet need populations. AGT is the most upstream precursor in the Renin-Angiotensin-Aldosterone System (RAAS), a cascade which has a demonstrated role in blood pressure regulation and its inhibition has well-established antihypertensive effects. Zilebesiran inhibits the synthesis of AGT in the liver, potentially leading to durable reductions in AGT protein and ultimately, in the vasoconstrictor angiotensin (Ang) II. Zilebesiran utilises Alnylam's Enhanced Stabilization Chemistry Plus (ESC+) GalNAc-conjugate technology, which enables infrequent subcutaneous dosing with increased selectivity and the potential to achieve tonic blood pressure control demonstrating consistent and durable blood pressure reduction throughout a 24-hour period, sustained up to six months after a single dose of zilebesiran.

In 2023, Roche and Alnylam entered a global partnership to co-develop and co-commercialise the RNAi therapeutic zilebesiran. As a part of this agreement, Alnylam and Roche will co-commercialize zilebesiran in the U.S. Outside the U.S., Roche has exclusive commercialisation rights, Chugai has obtained commercial rights in Japan under its license agreement with Roche. The safety and efficacy of zilebesiran have not been established or evaluated by the FDA, PMDA or any other health authority.

About RNAi therapeutics

RNAi (RNA interference) is a natural cellular process of gene silencing that represents one of the most promising and rapidly advancing frontiers in biology and drug development today. Its discovery was recognized with the award of the 2006 Nobel Prize for Physiology or Medicine. RNAi therapeutics is harnessed the natural biological process of RNAi occurring in our cells. Small interfering RNA (siRNA), the molecules that mediate RNAi and comprise Alnylam's RNAi therapeutic platform, function upstream of today's medicines by potently silencing messenger RNA (mRNA) – the genetic precursors that encode for disease-causing or disease pathway proteins – thus preventing them from being made.

Sources

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