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EMERGING COMPANY PROFILE

APRINOIA TACKLES TAU

BY CHRIS LIEU, STAFF WRITER

Aprinoia Therapeutics Inc. is developing a pipeline targeting tauopathies that includes diagnostic imaging tracers, mAbs specific to pathologic tau and small molecules that bind to tau rather than dissociate tau aggregates.

"We are going to develop imaging biomarkers for all the therapeutic targets first to see those targets, and then find therapies," CEO Ming-Kuei Jang told BioCentury.

The company's lead diagnostic, APN-1607, is a second-generation tau PET imaging compound in Phase I testing. Aprinoia, which has exclusive, worldwide rights to the tau tracer technology from National Institutes for Quantum and Radiological Science and Technology, optimized APN-1607 to increase its half-life by improving blood pharmacokinetics and metabolism, according to Jang.

In unpublished pilot clinical data, APN-1607 bound to three-repeat (3R) and 4R tau and differentiated multiple tau-associated disorders including Alzheimer's disease, progressive supranuclear palsy (PSP) and corticobasal degeneration (CBD). Disease progression in AD and PSP was also characterized by APN-1607 binding.

According to Jang, while other tau tracers may be useful for detecting AD, they may not detect rare tauopathies such as PSP or frontotemporal dementia. "In all the tauopathy patients we've scanned, we can see a signal and tracer retention in the location we expect to see tau pathology," he said.

Jang said the company compared APN-1607 with tau tracers flortaucipir from Eli Lilly and Co. and MK-6240 from Merck & Co. Inc. and Cerveau Technologies Inc. *In vitro* binding assays, radioligand binding assays on AD brain lysates and PET imaging in tau transgenic animal models suggested APN-1607 binds to a different binding pocket on tau than the other compounds.

Jang told BioCentury that it is unclear why APN-1607 behaves differently than these other agents but added that APN-1607 may recognize a specific tau species not recognized by other tracers that is present in all tauopathies or that the binding pocket could occur in all tau species across disease types.

APRINOIA THERAPEUTICS INC., TAIPEI, TAIWAN
Technology: Imaging and therapeutic compounds for neurodegenerative diseases

Disease focus: Diagnostic, neurology

Clinical status: Phase I

Founded: 2015 by Ming-Kuei Jang, Makoto Higuchi and Michael Hui

University collaborators: National Institutes for Quantum and Radiological Science and Technology

Corporate partners: Undisclosed

Number of employees: 27

Funds raised: $17.5 million

Investors: DCI Partners (Daiwa Securities), KTB Network, ShangPharma Group and WealthPath Investment

CEO: Ming-Kuei Jang

Patents: 8 issued for tau imaging tracer APN-1607 in several countries

This month, Lilly announced flortaucipir met the co-primary endpoints of predicting tau pathology and AD diagnosis in the Phase III A16 study. Merck's MK-6240 is in Phase I testing. Lilly's product is the most advanced tau tracer in the clinic.

Next year, Aprinoia plans to begin U.S. Phase II testing of APN-1607 in AD as well as PSP, for which the tracer has FDA Orphan Drug designation.

Aprinoia's APN-1701, a third-generation tau PET imaging compound, is slated for clinical testing this year and an α-synuclein PET imaging compound is slated to enter the clinic next.

The company is also developing therapeutics targeting intracellular tau with small molecule tau inhibitors and extracellular tau with anti-tau antibodies. While other companies are targeting a specific tau epitope, Aprinoia screens antibodies against full length tau aggregates and tau proteins derived from tauopathy patients.

"The goal is to find a diversity of tau antibodies that can recognize different forms of pathological tau," Jang said, adding that Aprinoia's antibodies recognize pathological tau in AD and PSP, and do not target normal tau.

In unpublished preclinical data, lead mAb APNmAb005 bound to pathological tau in AD and PSP brains as well as in brains of tau transgenic mice.

Aprinoia does not have a lead small molecule yet but Jang told BioCentury the company is developing tau binders that can stabilize and stop the spread of tau aggregates — rather than dissociate the aggregates — or prevent the interaction of downstream effectors.

Jang said that since the company has a way to target tau through its tracers, it can use therapeutic chemical moieties and combine the mAb and small molecules to target the different tau species. The company hopes to begin clinical testing of its tau therapeutics in 2020.

In January, Aprinoia raised $11 million in a series B round and hopes to raise $30-$40 million in a series C by year end. bc

COMPANIES AND INSTITUTIONS MENTIONED

Aprinoia Therapeutics Inc., Taipei, Taiwan
Cerveau Technologies Inc., Boston, Mass.
Eli Lilly and Co. (NYSE:LLY), Indianapolis, Ind.
Merck & Co. Inc. (NYSE:MRK), Kenilworth, N.J.
National Institutes for Quantum and Radiological Science and Technology, Chiba, Japan

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