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Daiichi In Massive $22bn Global Deal With Merck & Co For Three ADCs

New Validation Of DXd Platform

by Lisa Takagi

The two firms will co-develop and co-commercialize three Daiichi ADCs globally outside Japan in a deal the Japanese firm said would allow “more aggressive development plans targeting broader patient populations.”

In another big endorsement of its proprietary R&D platform, *Daiichi Sankyo Co., Ltd.* has announced a huge new global deal for three antibody-drug conjugate (ADC) candidates with *Merck & Co., Inc.*, worth $4bn upfront ($3bn immediately upon execution) and up to $22bn in total.

The agreement covers the Japanese firm's anti-HER3 ADC patritumab deruxtecan (HER3-DXd/U3-1402), anti-B7-H3 ADC ifinatamab deruxtecan (I-DXd/DS-7300) and CDH6-targeting ADC raludotatug deruxtecan (R-DXd/DS_6000), which will be jointly developed and commercialized worldwide except in Japan, where Daiichi retains exclusive rights.

Ex-Japan profits and expenses will be split equally, with Daiichi to "generally" book sales worldwide; potential aggregate revenues from the programs for each company will be at the "multi-billion dollar" level approaching the mid-2030s, the partners said.

It addition to the $4bn upfront and up to $1.5bn in continuation payments over the next 24 months, the agreement is worth up to $16.5bn in total contingent future sales milestones, with an additional refundable upfront payment of $1bn to Daiichi for future R&D expenses. Daiichi notes Merck will be responsible for up to the first $1.5bn in R&D expenses including $500,000 each for patritumab and ifinatamab, and 75% of the R&D costs for raludotatug.

Patritumab US BLA Expected By Next April

Positive results from the Phase II HERTHENA-Lung01 study with patritumab for patients with EGFR-mutated, locally advanced or metastatic non-small cell lung cancer (NSCLC) following disease progression with an EGFR TKI and platinum-based chemotherapy were announced in September. (Also see "*Daiichi Sankyo Comes Out Swinging At WCLC As ADCs Steal Show*" - Scrip, 11 Sep, 2023.) (Also see "*Big Readouts For AstraZeneca, Daiichi Sankyo And Gilead At Lung Cancer Congress*" - Scrip, 4 Sep, 2023.)

The candidate was granted Breakthrough Therapy Designation by the US Food and Drug Administration (FDA) in December 2021 for the treatment of patients with EGFR-mutated locally advanced or metastatic NSCLC with disease progression on or after treatment with a third-generation TKI and platinum-based therapies. At present, a US biologics license application in this setting is planned by the end of March 2024, based on data from HERTHENA-Lung01.

Ifinatamab is moving through the Phase II IDeate-01 study, investigating it as a monotherapy for patients with previously-treated, extensive-stage small cell lung cancer (SCLC).

Raludotatug, meanwhile has been in a Phase I trial for advanced renal cell carcinoma and advanced ovarian cancer, with the latest data in the second indication presented at this years European Society for Medical Oncology Congress.

Demand For Development Acceleration, Larger Markets

Collaboration with Merck/MSD “will help us deliver on our obligation to deliver these potential new DXd ADCs to more patients as quickly as possible,” Daiichi CEO Sunao Manabe said. Merck CEO Robert Davis said the deal helps the firm "augment and diversify our oncology pipeline while building on our immuno-oncology foundation."

Manabe pointed to Merck's “remarkable oncology experience and strong in-house development capabilities and resources” as represented by its blockbuster immuno-oncology drug Keytruda (pembrolizumab), which received US accelerated approval in 2021 in combination with Daiichi’s ADC Enhertu (trastuzumab deruxtecan) for the first-line treatment of locally advanced, unresectable or metastatic HER2 positive gastric or gastroesophageal junction adenocarcinoma.

Behind the new deal was a demand by Daiichi for enhanced capacity, resources and capabilities in order to maximize its DXd-ADC franchise, the firm noted. It added the collaboration enables “more aggressive development plans targeting broader patient populations,” accelerating development timelines in a global setting.

While several firms showed interest in collaborations for its ADC assets, Merck offered the highest valuation for the three candidates, it added. Daiichi's ADC platform attaches antibodies to topoisomerase I inhibitor payloads (the exatecan derivative DXd) via tetrapeptide-based cleavable linkers.

Including the assets in the Merck deal, six ADCs based on the platform are currently in clinical development.

The new deal will also allow Daiichi to allocate more resources to other pipeline ADCs including the tumor-associated mucin-1-directed DS-3939 in Phase I/II trial for advanced solid cancers, and the second-generation ADC DS-9609 against an undisclosed target.

(With contributions from Ian Haydock in Tokyo.)