COMPANY RESEARCH AND ANALYSIS REPORT

Chordia Therapeutics Inc.

190A

Tokyo Stock Exchange Growth Market

12-Dec.-2024

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https://www.chordiatherapeutics.com/en/ir.html

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Summary

Bio-venture advancing development of anti-cancer drugs with blockbuster potential

Chordia Therapeutics Inc. <190A> (hereafter, also "the Company") is a bio-venture specializing in small-molecule anti-cancer drug development established as a spin-out by drug discovery researchers from Takeda Pharmaceutical <4502>. With drug discovery through clinical research as its core business, the Company aims for monetization early on by handling manufacturing and sales in-house through strategic partnerships in Japan and out-licensing overseas. It listed on the Tokyo Stock Exchange Growth Market in June 2024.

1. Development pipeline status

The Company currently has five development pipelines, with its lead pipeline being the CLK inhibitor CTX-712 (hereafter, "CTX-712"). CTX-712 is undergoing Phase 1/2 clinical trials (currently in the Phase 1 part) in the US for hematologic malignancies (second- and later-line treatment of acute myeloid leukemia (AML)). CTX-712 is a small-molecule compound with a novel mechanism of action whereby excessive stress is applied during the mRNA* maturation process to kill cancer cells, and a Phase 1 clinical trial in Japan demonstrated safety and efficacy comparable to therapies submitted for approval. The Company apparently looks to submit an application for orphan drug designation in the US in 2024, and announce interim results from the Phase 1 part in the latter half of 2025. It plans to conduct the Phase 2 part in the US and Japan and collect clinical trial data by the end of 2026 if it goes well, with the aim of a New Drug Application (NDA) submission in 2026-2028 utilizing the accelerated drug approval program. The Company estimates a potential market size of ¥200.0bn-¥400.0bn for second- and later-line therapies for AML. If it succeeds in developing CTX-712 for those indications, it aims to maximize the product's value by pursuing expansion of indications to first-line treatment for AML, other types of cancer, and so forth.

* RNA stands for ribonucleic acid, a substance needed to make proteins from DNA, a gene. Types of RNA include messenger RNA (mRNA) transcribed from genomic DNA, and transfer RNA (tRNA) used during protein synthesis.

2. Results trends

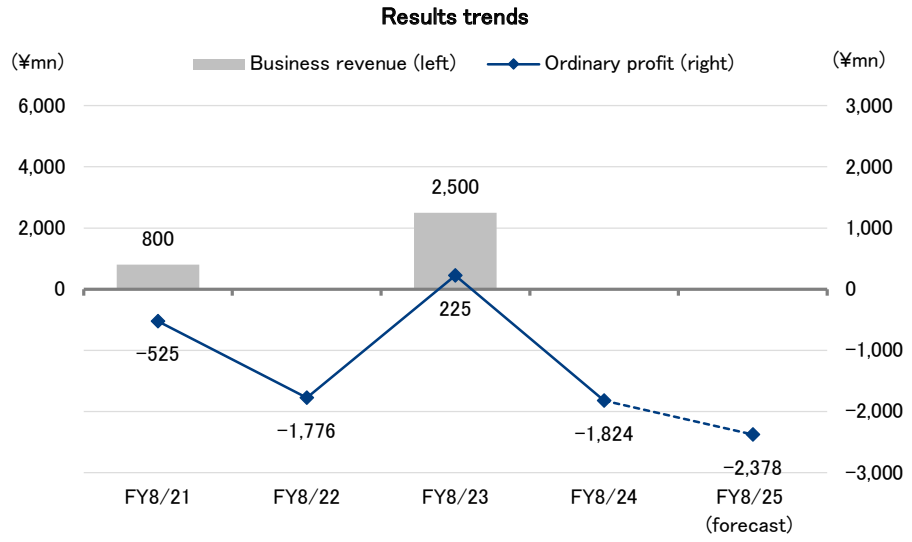
As for FY8/24 results, no business revenue was recorded (milestone income of ¥2,500mn from Ono Pharmaceutical Co., Ltd., licensee of the MALT1 inhibitor CTX-177, was recorded in the previous fiscal year), and there was ordinary loss of ¥1,824mn (profit of ¥225mn in the previous fiscal year). In FY8/25, the Company does not expect to record business revenue either at present, and forecasts ordinary loss will increase to ¥2,378mn due to growth in clinical trial expenses for CTX-712. It had cash and deposits totaling ¥4,329mn at the end of August 2024, which is enough to fund nearly two years of business activities, but plans to obtain funds for development from the equity market if needed since upfront investment will continue for the foreseeable future. It intends to ensure funds for at least one year of business activities.

3. Management policies going forward

The Company's vision for 2030 is "To be an R&D-oriented pharmaceutical company based in Japan." It is establishing frameworks therein, including by entering in 2022 into basic agreements for business partnerships with Shionogi Pharma Co., Ltd. in pharmaceutical manufacturing and MEDIPAL HOLDINGS CORPORATION <7459> in domestic distribution and sales activities. Under its strategy for overseas markets of out-licensing with the aim of early monetization, CTX-177 licensed out to Ono Pharmaceutical in 2020 is currently in a Phase 1 clinical trial for relapsed and refractory lymphomas in the US. The Company is also considering out-licensing the three remaining pipelines early on at the pre-clinical trial stage, and targets early monetization by focusing resources on CTX-712's development for the foreseeable future.

Key Points

- Spin-out from Takeda Pharmaceutical to specialize in small-molecule anti-cancer drug development
- Targets NDA submission around 2026-2028 for CTX-712 undergoing clinical trial in the US for second-line and later treatment of acute myeloid leukemia
- Out-licensed MALT1 inhibitor to Ono Pharmaceutical for up to just over ¥50.0bn
- Focuses resources on maximizing CTX-712's value, targeting early monetization



Source: Prepared by FISCO from the Company's financial results and website

Company overview

Spin-out from Takeda Pharmaceutical to specialize in small-molecule anti-cancer drug development

1. Company history

Chordia Therapeutics is a bio-venture established in October 2017 as a spin-out by six drug discovery researchers who had been working on small-molecule anti-cancer drug development at Takeda Pharmaceutical. The six founders selected four of the pipelines they had worked on developing at Takeda Pharmaceutical, entered into a license agreement with Takeda Pharmaceutical in November 2017 for exclusive worldwide rights to research, develop, manufacture, and commercialize them, and commenced development. When Takeda Pharmaceutical was rethinking its overall R&D strategy for the Group around 2016, it decided to streamline in-house development of anti-cancer drugs to new modalities like antibody drugs and cell therapy, and place less priority on the development of small-molecule compounds. This decision was motivated by a need for business selection and concentration, not because low-molecule compound drug discovery was no longer promising. Against this backdrop, current Chordia Therapeutics CEO Hiroshi Miyake who was the Japan site head of the oncology drug discovery unit at Takeda Pharmaceutical at the time joined others to establish a spin-out and continue small-molecule compound drug discovery. The economic terms and conditions under the license agreement with Takeda Pharmaceutical are apparently more favorable for Chordia Therapeutics than typical economic terms, partly reflecting the background to its establishment and because Takeda Pharmaceutical is its principal shareholder with a roughly 16% stake.

For Chordia Therapeutics' lead pipeline CTX-712, a Phase 1 clinical trial began in Japan in August 2018, followed by the start of a Phase 1/2 clinical trial in the US in February 2023. In addition, in December 2020, the Company entered into a worldwide exclusive license agreement for CTX-177 with Ono Pharmaceutical (upfront payment of ¥0.8bn and development and commercial milestones up to ¥52.1bn, sales royalties in the upper-single-digit to lower-double-digit percent range). Ono Pharmaceutical started CTX-177's Phase 1 clinical trial in the US in August 2022.

Chordia Therapeutics aims to develop business as a pharmaceutical company in the Japan market. As frameworks for that purpose, it concluded in May 2022 both a basic agreement on collaboration in manufacturing with Shionogi Pharma, and a basic agreement on collaboration in distribution and sales promotion with MEDIPAL HOLDINGS. Chordia Therapeutics had 22 employees (including 12 Ph.D.s) as of August 31, 2024, and plans to maintain that level for the foreseeable future.

Company history

Date	Key event
October 2017	Established Chordia Therapeutics Inc. in Shonan iPark, Fujisawa City, Kanagawa Prefecture to conduct drug discovery research
November 2017	Entered into a license agreement with Takeda Pharmaceutical Company Limited to acquire exclusive worldwide rights to research, develop, manufacture, and commercialize four pipelines Entered into an investment agreement with Takeda Pharmaceutical Company Limited, Kyoto University Innovation Capital Co., Ltd., and other underwriters
August 2018	Commenced Phase 1 clinical trial for the anti-cancer compound CTX-712 in Japan
March 2019	Entered into an investment agreement with JAFCO Group Co., Ltd., Kyoto University Innovation Capital Co., Ltd., and other underwriters
December 2020	Entered into a license agreement with Ono Pharmaceutical Co., Ltd. to grant it exclusive worldwide rights to research, develop, manufacture, and commercialize the Company's anti-cancer compound CTX-177 and its related compounds
May 2022	Entered into an investment agreement underwritten by Japan Growth Capital Investment Corporation, UTokyo Innovation Platform Co., Ltd., MEDIPAL Innovation Fund, Shinsei Capital Partners, Ltd., Nippon Venture Capital Co., Ltd., and Shionogi Pharma Co., Ltd. Concluded a basic agreement with MEDIPAL HOLDINGS CORPORATION regarding a future business alliance in areas such as distribution and sales promotion Concluded a basic agreement with Shionogi Pharma Co., Ltd. regarding collaboration in manufacturing small-molecule compounds
August 2022	Commenced Phase 1 clinical trial for the anti-cancer compound CTX-177 (ONO-7018) in the US through the licensee Ono Pharmaceutical Co., Ltd.
February 2023	Commenced Phase 1/2 clinical trial for the anti-cancer compound CTX-712 in the US
August 2023	Completed patient enrollment for Phase 1 clinical trial of the anti-cancer compound CTX-712 in Japan
June 2024	Listed on the Tokyo Stock Exchange Growth Market

Source: Prepared by FISCO from the Company's prospectus for the issuance of new shares and secondary offering of shares and results briefing materials

Developing cancer therapies targeting RNA deregulation stress

2. Business overview

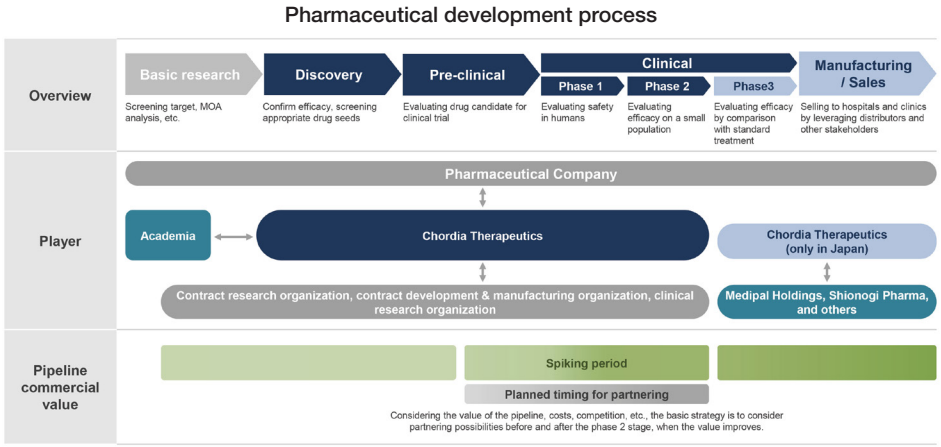
(1) Management policies

The Company's aim is "Building a world where tomorrow is another day" by developing and delivering ground-breaking new anti-cancer drugs from Japan to patients as soon as possible. Its mission is to develop first-in-class anti-cancer drugs, and its vision for 2030 is to grow into an R&D-oriented pharmaceutical company based in Japan by achieving that.

(2) Business model

Chordia Therapeutics' hallmarks are its ability to search for seeds through collaboration with academia and bring drugs to market with drug discovery capabilities cultivated at a pharmaceutical company. It is efficiently advancing collaborative research with academia while utilizing subsidies from the Japan Agency for Medical Research and Development (hereafter, "AMED"), as well as working to make development more efficient by utilizing Fujitsu's AI technology to discover biomarkers that are important in new drug development.

Pharmaceutical development starts with basic research, followed by discovery and pre-clinical research before moving on to clinical trials to confirm safety and efficacy in humans. After that, manufacturing and marketing approval is obtained to bring the drug to market. The Company's basic policy is to position its core business as the part of this process from discovery through Phase 2 clinical trials (evaluation of efficacy in a small number of patients). In addition, it will handle manufacturing and sales in-house in Japan, while utilizing out-licensing in overseas markets. As for the timing of out-licensing, it will consider it around Phase 2 clinical trials when value increases as a basic pattern, reflecting the pipeline's value, costs, and competitive conditions.



Source: The Company's results briefing materials

Chordia Therapeutics is working to discover first-in-class*, small-molecule compounds in its target field of oncology where there are strong medical needs. Although predicting safety and efficacy is difficult due to their novel mechanisms of action, these compounds also have the potential to deliver significant therapeutic effects to patients for which existing treatments have been ineffective. Global pharmaceutical companies are also very interested in these compounds since prices for them are often set high according to their efficacy and novelty when calculating drug prices, which is conducive to major license agreements. Chordia Therapeutics is conducting such drug discovery research in collaboration with many academia, and is distinct in that it is proceeding efficiently while utilizing subsidies from AMED on the financial front.

* Innovative pharmaceuticals demonstrating effectiveness differing from existing treatments through a new and unique mechanism of action

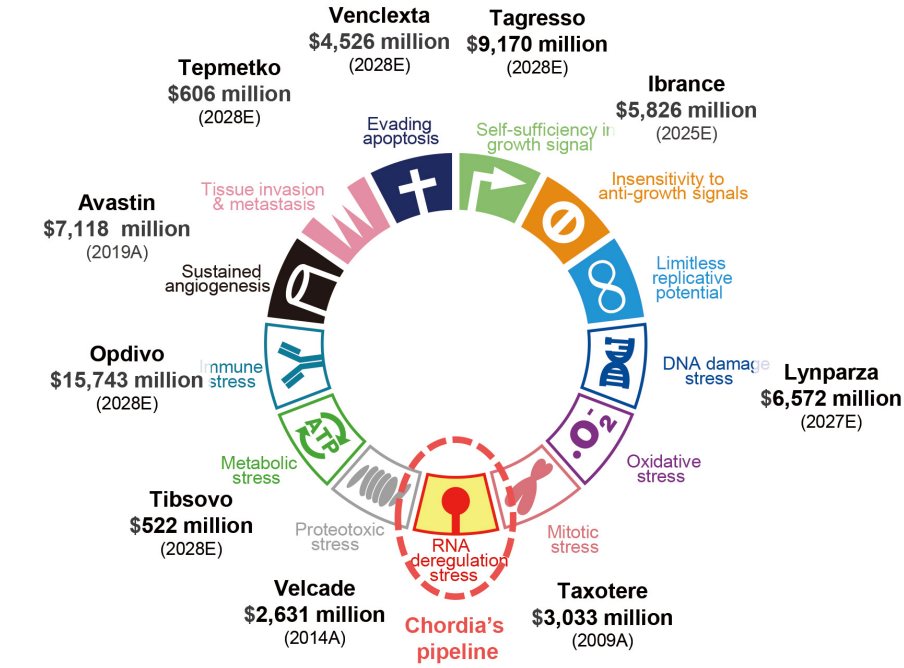
Source: The Company's results briefing materials

(3) Anti-cancer drugs targeting RNA deregulation stress

Discovering hallmarks of cancer and identifying differences from normal cells is considered important for finding molecules for anti-cancer drugs to target. Research in recent years has identified 13 hallmarks of cancer, and Ono Pharmaceutical's Opdivo is among numerous blockbuster anti-cancer drugs targeting one of those hallmarks, immune stress, that have been developed. Against this backdrop, Chordia Therapeutics is working to develop anti-cancer drugs targeting RNA deregulation stress, which have yet to be launched.

RNA deregulation stress

Thirteen cancer hallmarks & typical drugs with peak sales(1)

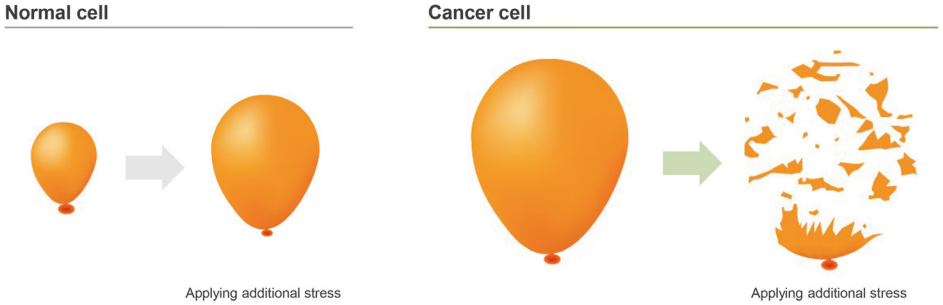


Source: The Company's results briefing materials

Cancer cells are under extreme stress compared to normal cells because of multiple disruptions during RNA generation. Administering anti-cancer drugs that apply even more stress to the overstressed cancer cells kills them. Although administering anti-cancer drugs also puts some stress on unstressed normal cells and produces modest effects*, research has shown that they return to normal as the stress is relieved over time.

* In the Phase 1 clinical trial of CTX-712, side effects such as nausea and vomiting were observed but were controllable with the administration of antiemetic agents, and the safety profile was acceptable.

Concept for anti-cancer drugs

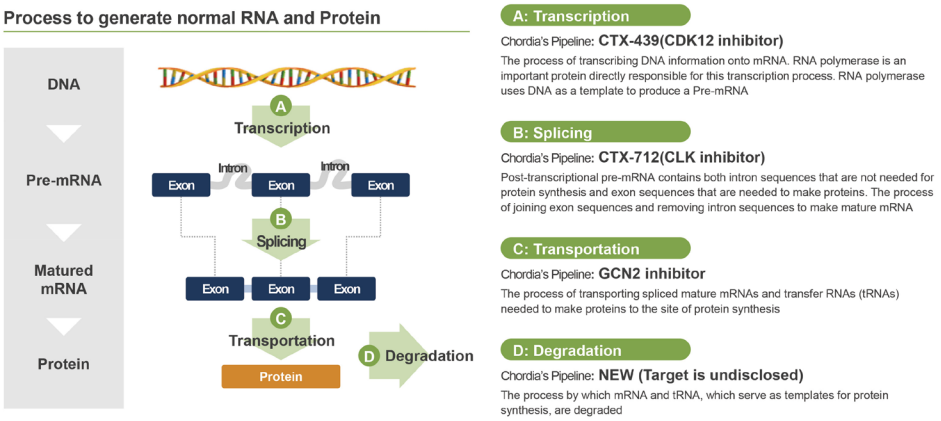


Source: The Company's results briefing materials

Taking a brief look at protein generation in humans, genetic information from DNA is transcribed to generate precursor mRNA, which next undergoes the necessary splicing*1 to become mature mRNA, after which protein is generated by transporting transfer RNA to the site of protein synthesis. Chordia Therapeutics is working to develop anti-cancer drugs that inhibit various types of kinase*2 that play a role in these processes including transcription, splicing, and transportation.

*1 Process of removing from precursor mRNA the parts that are not necessary (introns) in protein synthesis.
*2 Kinase is a general term for enzymes that regulate cell proliferation and other functions.

RNA generation process and Chordia Therapeutics' pipeline modes of action



Source: The Company's results briefing materials

Development pipelines

CTX-712 is in clinical trial in the US for second-line and later treatment of acute myeloid leukemia, NDA submission targeted around 2027

1. CTX-712 (CLK inhibitor)

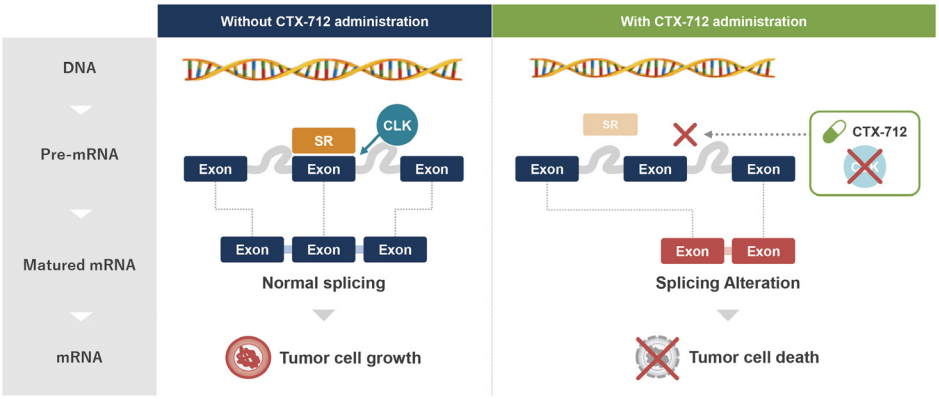
(1) Development status

CTX-712 (CLK inhibitor) is currently the lead pipeline. It causes splicing alterations by inhibiting the activity of CLK kinase*, which plays an important role in the mRNA maturation process. This increases RNA deregulation stress, which is expected to kill cancer cells.

* CLK kinase phosphorylates SR proteins. Phosphorylated SR proteins promote normal splicing by accurately removing unnecessary sections (introns) of pre-mRNA.

Development pipelines

CTX-712's effects



Source: The Company's results briefing materials

In a Phase 1 clinical trial in Japan from 2018 to 2023, safety and efficacy were demonstrated in a total of 60 patients lacking effective standard treatment options with acute myeloid leukemia (hereafter, "AML"), myelodysplastic syndrome (hereafter, "MDS")*1, as well as other solid cancers (ovarian cancer, breast cancer, pancreatic cancer, colorectal cancer, sarcoma, etc.). As for the trial design, a dose escalation study with twice-a-week administration*2 was conducted, and data was collected and evaluated on safety, efficacy to determine maximum tolerated dose, and dose-limiting toxicity as the primary endpoints, as well as pharmacokinetics and other secondary endpoints.

*1 MDS is a disorder wherein normal blood cells (red blood cells, white blood cells, platelets) can be poorly produced due to abnormalities in hematopoietic stem cells from which blood cells in bone marrow develop, and sometimes MDS progresses to AML.
*2 Dosing is used to restore the condition of normal cells subjected to stress from the administration of CTX-712.

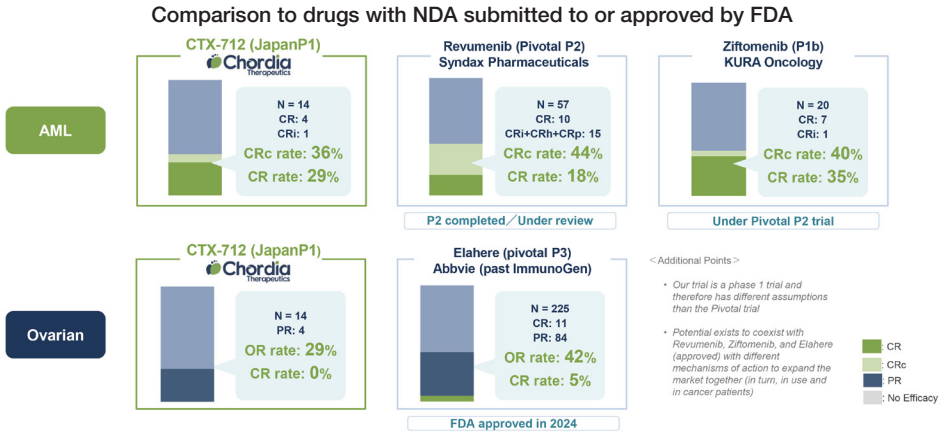
During the course of administration to trial subjects, therapeutic effects were observed in hematologic malignancies, ovarian cancer, and so forth, so enrollment of those patients was prioritized. As a result, 14 patients with hematologic malignancies, 14 patients with ovarian cancer and, 32 patients with other solid cancers were enrolled in the study. Results of the clinical trial (data through November 2023) were announced at the American Association for Cancer Research Annual Meeting in April 2024. Although adverse events such as nausea, vomiting, and diarrhea were observed, they were controllable with the administration of medication such as antiemetic agents as previously mentioned, and the safety profile was acceptable.

Regarding efficacy, PR (Partial Response)*1 was achieved in 4 out of 14 ovarian cancer patients, and of a total of 14 AML and MDS patients (including 12 AML patients), CR (Complete Remission) was achieved in 4 patients, CRi (Complete Remission with Incomplete hematologic recovery) was achieved in 1 patient, and MLFS (Morphologic Leukemia-Free State) was achieved in 1 patient. The overall response rate was 43% and the CR rate was 29%*2. These levels of efficiency are comparable to Phase 1 clinical trial results*3 for Ono Pharmaceutical's Opdivo, which became a blockbuster anti-cancer drug, and Daiichi Sankyo's <4568> VANFLYTA, which was approved as an AML drug. In addition, the results are comparable to ovarian cancer drugs and AML drugs for which NDA has recently been submitted to or approved by the FDA. Chordia Therapeutics regards the results as promising for a future launch.

*1 PR (Partial Response) denotes a 30% or greater reduction in the tumor diameter compared to before treatment. In leukemia, CR (Complete Remission) denotes that the bone marrow contains less than 5% leukemic cells and the number of normal neutrophils and platelets has been completely restored. CRi (Complete Remission with Incomplete hematologic recovery) denotes the bone marrow contains less than 5% leukemic cells, but neutrophils and/or platelets have not fully recovered. MLFS (Morphologic Leukemia Free State) denotes that no leukemic cells are found in a bone marrow examination (undetectable by optical microscopy).

*2 Tumor shrinkage was observed for roughly half of the remaining solid cancer patients but was not sufficient to achieve PR.

*3 For VANFLYTA, none of 16 patients achieved CR but 56% of them achieved some kind of response (overall response rate 56%). In the Phase 1 clinical trial for Opdivo, 1 out of 4 patients achieved CR for melanoma (overall response rate 25%) for which the drug was first approved.



Source: The Company's results briefing materials

CTX-712 induced splicing abnormalities in all of the subjects to which it was administered. Also, 3 of the 4 subjects with splicing factor mutations among the 14 subjects with AML and MDS achieved a response, and the treatment duration for all 3 of them was 300 days or longer, demonstrating a long-term response and otherwise showing a strong correlation between these patients' splicing abnormalities and therapeutic effects. Looking at the ratio of patients with splicing factor mutations by cancer type, it tends to be relatively high for hematologic malignancies at 10-20% for AML and 40% for MDS, compared to a low 1-2% for lung, breast, and other types of cancer. Moreover, AML has a high rate of relapse as standard treatments prove ineffective and a low 5-year survival rate of about 30%, so it is a field where the development of novel therapies is strongly desired. Given this situation, Chordia Therapeutics decided to first work on developing CTX-712 for indication as a second- and later-line treatment for AML, and began a Phase 1/2 clinical study in the US in 2023*.

* Phase 1 is also being conducted in the US because a capsule formulation was used in the clinical trial in Japan, whereas a tablet formulation is being used in the clinical trial in the US with a view to marketing.

Chordia Therapeutics had planned to complete the Phase 1 part of the clinical trial in the US around the end of 2024 and announce the interim results in mid-2025, but pushed back its outlook for the release of interim results to around the end of 2025 because it changed course*1 to increase patient enrollment in the Phase 1 study in line with Project Optimus*2 proposed by the FDA three years ago. The Company initially planned on enrolling about 20 patients (once-weekly dose escalation study) in the Phase 1 part out of planned total enrollment of 140-170 patients in the Phase 1/2 clinical trial, but is now discussing revisions to its protocol to add a twice-weekly dose escalation study. Enrollment of 20 patients in the once-weekly dosing group was completed as of August 31, 2024, and, although the Phase 1 part will be pushed back by about six months to one year from the initial schedule due to the additional inclusion of twice-weekly dosing, the overall schedule is apparently largely unchanged as total patient enrollment will remain about the same (patient enrollment for Phase 2 will decrease), and the Company expects to announce the final results at the end of 2026 if patient enrollment proceeds smoothly.

*1 Chordia Therapeutics changed its course based on advice from a consulting company that complying with Project Optimus guidelines is preferable in order to obtain marketing approval after the Phase 2 clinical trial since there have been cases in the US where other companies attempted to submit NDAs for development products not compliant with the guidelines, but they were rejected by the FDA.
*2 The FDA provided guidance recommending conducting Phase 2 clinical trials after examining several dosage and administration regimens during Phase 1 to increase safety and optimize dosage in the development of anti-cancer drugs.

The Company has decided to hold discussions with the PMDA so that the Phase 2 part can be conducted not only in the US but also in Japan. In the US, the Company plans to submit an orphan drug designation request for a potential rare disease treatment within 2024, and submit an NDA if the results of the Phase 2 clinical trial are good. In Japan, it plans to use the SAKIGAKE Designation System* to file for approval after the Phase 2 clinical trial. If all goes well, a launch in Japan and the US is possible in 2028.

* This is system wherein the Ministry of Health, Labour and Welfare (MHLW) designates products in development that meet specified criteria, such as the innovativeness of the medication, the severity of the target disease, very high efficacy for the target disease, and the intent and framework for early development and filing for approval in Japan ahead of other countries (or at the same time), as SAKIGAKE pharmaceuticals, with the aim of early practical application by conducting priority reviews, consultations, and so forth (aims to shorten the review period from the normal one year to six months).

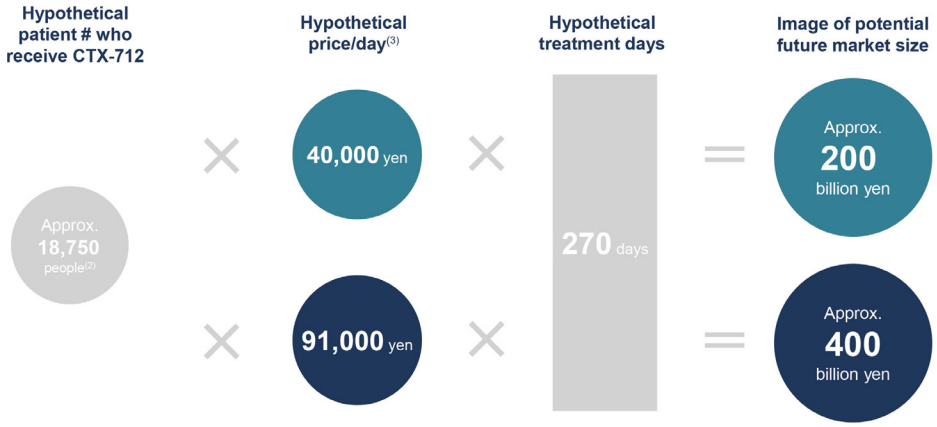
(2) Potential market scale as second- and later-line treatment for AML

The number of AML patients is estimated at 50,000 a year in major countries in Japan, the US, and Europe. Some of them do not respond to first-line treatment or relapse, and proceed to second-line treatment. The probability of that is seen as up to 50%, and CTX-712's initial target is patients among them without actionable genetic mutations (FLT3, IDH1/2, etc.) for which treatments are available and patients that move on to third-line treatments after second-line treatments prove ineffective. Chordia Therapeutics estimates the target patient population at up to about 18,000.

Multiplying this prospective number of patients by the price/day referencing existing therapies (¥40,000-¥91,000) and average treatment period (estimated about 270 days) puts the potential market scale at ¥200.0bn-¥400.0bn. If CTX-712 is approved for marketing as a second-line and later treatment for AML, the Company's strategy is to work to gradually expand its indications to first-line treatment for AML and other types of cancer, so it has the potential to grow into a blockbuster.

Development pipelines

Estimated market scale as second- and later-line treatment for AML



Source: The Company's results briefing materials

(3) Development strategy and potential market scale for ovarian cancer

For ovarian cancer drug therapy, TC treatment combining a platinum-based drug and a taxane-based drug are widely used as a standard treatment, and drugs targeting molecules characteristic of cancer cells have also been developed. Therefore, the Company plans on development initially targeting patients with relapsed and refractory platinum-resistant ovarian cancer with limited treatment options beyond third-line therapy, and has yet to determine a specific schedule. The Company estimates a target patient population in major countries in Japan, the US, and Europe of around 19,000. Also, the Company estimates the potential market scale at ¥100.0bn-¥200.0bn based on the projected patient numbers and hypothetical assumptions for the price/day (¥40,000-¥91,000) and average treatment period (about 135 days).

(4) Manufacturing and sales framework

The Company plans on in-house manufacturing and sales in Japan, and intends to outsource manufacturing to Shionogi Pharma with which it concluded a collaborative agreement in 2022. In addition, business partner MEDIPAL is to handle distribution and sales promotion activities. As for the US and other overseas markets, the Company plans to develop sales by concluding sales license agreements with global pharmaceutical companies, and has already entered into a non-disclosure agreement with and is providing information to several companies. As for the timing of license agreement conclusion, the Company will decide on candidate companies after reviewing the interim results of the Phase 1 part or the final trial results including the Phase 2 part. The Company looks to conclude license agreements with advantageous terms that maximize product value.

(5) Status of CLK inhibitor competitors

There are three bio-ventures in the US developing CLK inhibitors, but the Company does not view any of them at a threat at this point. Biosplice Therapeutics conducted a Phase 1 clinical trial with single-agent dosing but the overall response rate was 0% (six patients achieved a reduction in tumor size of 10% or more), and is currently just conducting a Phase 1 clinical trial with combination therapy for cancers such as prostate cancer and colorectal cancer, indicating that efficacy in patients is not being clearly demonstrated. Also, BlossomHill Therapeutics has started patient registration for a Phase 1 clinical trial for AML, but it appears to be about five years behind Chordia Therapeutics. Also, the drug it is developing is a multikinase inhibitor, which is seen as having a higher risk of side effects since CLK is not the only kinase inhibited. Redona Therapeutics is currently only at the stage of selecting candidates, so it will probably take some time for it to enter clinical trials.

Chordia Therapeutics is in the lead in CLK inhibitor development, and has already registered the substance patent in 51 major countries in the world. Therefore, focus will be on interim results from the Phase 1 part expected to be announced around the end of 2025 as big deals could follow if clinical trials show good results.

MALT1 inhibitor out-licensed to Ono Pharmaceutical for up to over ¥50.0bn

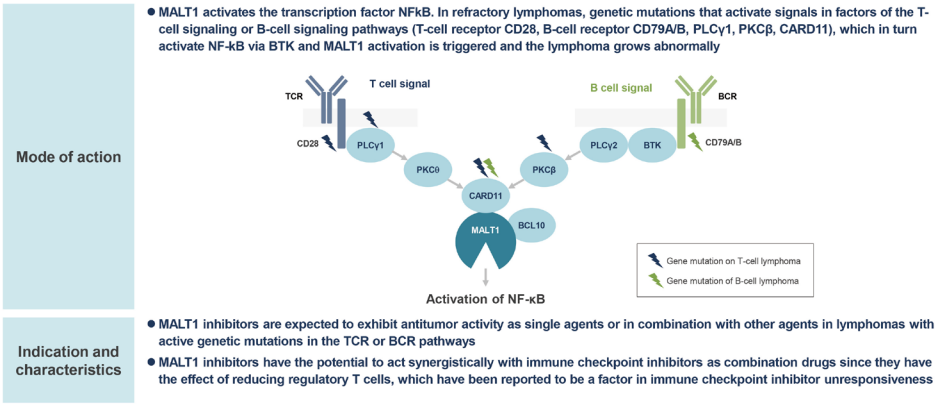
2. MALT1 inhibitor

(1) MALT1 inhibitor's mechanism of action and background to early out-licensing

The MALT1 inhibitor is a pipeline being developed as a promising therapy for refractory lymphomas, which Chordia Therapeutics out-licensed to Ono Pharmaceutical early-on after preclinical trials in 2020.

In refractory lymphomas, it is known that genetic mutations activate signals in factors of the T-cell signaling or B-cell signaling pathways (T-cell receptor CD28, B-cell receptor CD79A/B, PLCγ1, PKCβ, CARD11), and those signals trigger activation of NF-kB via BTK and MALT1 (Mucosa Associated Lymphoid Tissue protein 1), causing the lymphoma to grow abnormally.

MALT1 inhibitor



Source: The Company's results briefing materials

MALT1 inhibitors are expected to exhibit antitumor activity as single agents or in combination with other agents (BTK inhibitors, etc.) in lymphomas with active genetic mutations in such signaling pathways. Notably, MALT1 inhibitors also have the potential to act synergistically with immune checkpoint inhibitors as combination drugs since they have the effect of reducing regulatory T-cells, which have been reported to be a factor in immune checkpoint inhibitor unresponsiveness. Opdivo developer Ono Pharmaceutical licensing in the MALT1 inhibitor was very significant. Further, that Ono Pharmaceutical was marketing a BTK inhibitor was likely another reason for concluding the license agreement. That is because if multiple sites in the same signaling pathway can be inhibited, efficacy will be bolstered.

A key reason Chordia Therapeutics decided to out-license the agent early on is that Janssen, which was viewed as the industry leader in lymphoma treatments, started a Phase 1 clinical trial on a MALT1 inhibitor in 2019. After considering that it was 2-3 years behind Janssen and other factors including its financial situation, Chordia Therapeutics came to the business decision that early out-licensing would be better than in-house development.

(2) Economic terms of license agreement and development status

As for the economic terms of the license agreement, Chordia Therapeutics has already received an upfront payment of ¥0.8bn (FY8/21) and a first development milestone payment of ¥2.5bn (FY8/23) for starting the Phase 1 clinical study. The agreement also provides for up to an additional ¥49.6bn from future development and commercial milestones, and sales royalties in the upper-single-digit to lower-double-digit percent range.

Regarding the development status of ONO-7018 (CTX-177) at Ono Pharmaceutical, a Phase 1 study began in the US in August 2022 in patients with relapsed/refractory non-Hodgkin lymphoma or chronic lymphocytic leukemia (first patient enrolled in February 2023, targeted enrollment of 108 patients, study completion scheduled for the end of 2027*). In addition, a Phase 1 study in Japan began in August 2024 in patients with relapsed/refractory non-Hodgkin lymphoma (targeted enrollment of 24 patients, study completion scheduled for the end of 2029*). Incidentally, there are five MALT1 inhibitors at the Phase 1 clinical trial stage, including ONO-7018. Among them, Jansen's Safimaltib is currently a step ahead having completed patient registration.

* The source is ClinicalTrials.gov for the US, and Japan Registry of Clinical Trials portal site for Japan.

Aims to out-license other pipelines early on at the pre-clinical trial stage

3. Other pipelines

The Company's other pipelines are CTX-439 (CDK12 inhibitor) for solid cancers and a GCN2 inhibitor for hematologic malignancies, along with a new pipeline. However, its plan is to concentrate management resources on its top priority of achieving monetization early on by launching CTX-712. Therefore, it apparently intends to search for business partners so that it can out-license these other pipelines at the pre-clinical stage, as it has done with CTX-177. CTX-439 represses the transcription of mRNA via RNA polymerase II by inhibiting CDK12. Its mechanism of action is repressing this transcription of mRNA, causing abnormal mRNA to accumulate, and overstressed cancer cells to die. CTX-439's safety and efficacy in animals has already been demonstrated in a pre-clinical studies, and manufacturing of the investigational drug substance has been completed. It is currently in the stage of formulation consideration, and the Company will employ the data from the pre-clinical trial to advance license negotiations. The GCN2 inhibitor is in the discovery stage, and the Company aims to out-license it after conducting a pre-clinical trial.

Development pipelines

Program (target)	Lead indications (cancer type)	Region	Development status	Development and commercialization rights
CTX-712 (CLK)	AML/MDS, ovarian cancer, other solid cancers	Japan	Phase 1 clinical trial completed	In-house
	AML	US	Phase 1/2 clinical trial underway	In-house (searching for sales licensee)
CTX-177 (MALT1)	Lymphoid malignancies	US	Phase 1 part of clinical trial underway	Ono Pharmaceutical
CTX-439 (CDK12)	Solid cancers	-	Pre-clinical trial completed	In-house (aims to out-license early on)
(GCN2)	Hematologic malignancies, solid cancers	-	Discovery	In-house (aims to out-license early on)
New pipeline	Hematologic malignancies, solid cancers	-	Discovery	In-house (aims to out-license early on)

Source: Prepared by FISCO from the Company's results briefing materials

Results trends

No business revenue recorded, operating loss posted in FY8/24

1. FY8/24 results overview

In FY8/24, no business revenue was recorded (milestone income of ¥2,500mn was recorded in the previous fiscal year), and there was operating loss of ¥1,801mn (profit of ¥212mn in the previous fiscal year), ordinary loss of ¥1,824mn (profit of ¥225mn), and net loss of ¥1,827mn (profit of ¥223mn).

FY8/24 results

(¥mn)

	FY8/23 Results	FY8/24		YoY Change	Vs. plan Change
		Company plan	Results		
Business revenue	2,500	-	-	-2,500	-
Research and development expenses	1,996	1,948	1,499	-497	-448
CTX-712	686	-	1,018	331	-
CTX-177	3	-	0	-2	-
CTX-439	616	-	132	-483	-
Other (including personnel expenses)	690	-	347	-342	-
Other administrative expenses	291	324	301	10	-22
Operating profit	212	-2,273	-1,801	-2,013	471
Ordinary profit	225	-2,278	-1,824	-2,050	453
Net profit	223	-2,280	-1,827	-2,050	452

Source: Prepared by FISCO from the Company's financial results and results briefing materials

Research and development expenses declined ¥497mn year-on-year (YoY) to ¥1,499mn. As for the breakdown, expenses for CTX-712 rose ¥331mn YoY to ¥1,018mn due to the start of the Phase 1/2 clinical trial in the US, while those for CTX-439 declined ¥483mn to ¥132mn accompanying the completion of safety tests and manufacturing of the investigational drug, and other development expenses decreased ¥342mn to ¥347mn. Also, non-operating items were posted such as grant income of ¥17mn and stock listing expenses of ¥28mn.

Losses expected to continue in FY8/25 due to growth in CTX-712 development expenses

2. FY8/25 results forecasts

In FY8/25, the Company also plans to record no business revenue, and forecasts continued losses with operating loss of ¥2,434mn (¥1,801mn loss in the previous fiscal year), ordinary loss of ¥2,378mn (¥1,842mn loss), and a net loss of ¥2,380mn (¥1,827mn loss).

Results trends

FY8/25 results forecasts

(¥mn)

	FY8/24 Results	FY8/25 Company plan	YoY Change
Business revenue	-	-	-
Research and development expenses	1,499	2,025	525
CTX-712	1,018	1,610	592
CTX-177	0	0	-0
CTX-439	132	18	-114
Other (including personnel expenses)	347	396	49
Other administrative expenses	301	408	107
Operating profit	-1,801	-2,434	-633
Ordinary profit	-1,824	-2,378	-553
Net profit	-1,827	-2,380	-553

Source: Prepared by FISCO from the Company's results briefing materials

The Company forecasts research and development expenses will increase ¥525mn YoY to ¥2,025mn, mainly reflecting ¥1,610mn in expenses for CTX-712's Phase 1/2 clinical trial (including investigational drug manufacturing expenses). It expects research and development expenses for CTX-439 to decline to ¥18mn (assuming only expenses for activities granted by AMED) since it plans on out-licensing rather than in-house development as previously mentioned. It forecasts other administrative expenses, mainly expenses related to acquiring patents, will rise ¥107mn YoY to ¥408mn. In addition, the Company expects non-operating income and expenses to improve ¥80mn YoY, owing to the recording of ¥56mn in grant income from AMED (five programs) and the elimination of stock listing-related expenses. It expects research and development expenses to stay around the ¥2.0bn level for the foreseeable future since it intends to focus on advancing CTX-712's development.

Raised ¥1.4bn in funds by listing shares, policy for foreseeable future is to ensure enough cash on hand to fund one year of business activities

3. Financial position

Looking at the financial position at the end of FY8/24, total assets declined ¥276mn from the end of the previous fiscal year to ¥4,632mn. Although there was ¥1,464mn in proceeds from issuance of stock accompanying listing on the stock market, cash and deposits decreased ¥469mn alongside expenditures for business activities.

Total liabilities increased ¥62mn from the end of the previous fiscal year to ¥471mn. This mainly owes to a ¥133mn increase in accounts payable-other. In addition, net assets decreased ¥339mn to ¥4,161mn. Share capital and capital surplus each increased ¥755mn accompanying the issuance of shares, while retained earnings decreased ¥1,827mn due to the recording of a net loss.

The equity ratio, an indicator of management safety, was 89.8%, down 1.4 percentage points from the end of the previous fiscal year. Since it is difficult for a bio-venture without ongoing revenue to borrow from financial institutions, cash on hand will decrease for the time being as the development stage continues, although the Company does not have any outstanding interest-bearing debt. The Company had cash on hand of ¥4,329mn at the end of August 2024, but envisions that declining to around ¥2,000mn a year later at the end of FY8/25 since it forecasts net loss of ¥2,380mn in FY8/25. Regarding its cash position, the Company looks to ensure enough funds for one year of business activities, and will apparently obtain funds through equity financing if it looks like funds are going to fall below that level in the future.

Results trends

Balance sheet

(¥mn)

	End-FY8/22	End-FY8/23	End-FY8/24	Change
Current assets	4,482	4,891	4,605	-286
Cash and deposits	4,254	4,799	4,329	-469
Non-current assets	16	17	26	9
Total assets	4,498	4,909	4,632	-276
Total liabilities	221	408	471	62
Interest-bearing debt	-	-	-	-
Total net assets	4,277	4,500	4,161	-339
Safety				
Equity ratio	94.5%	91.2%	89.8%	-1.4 pp
Interest-bearing debt ratio	-	-	-	-

Source: Prepared by FISCO from the Company's financial results and prospectus for the issuance of new shares and secondary offering of shares

Focusing resources on maximizing CTX-712's product value, aiming for early monetization

4. Management policies going forward

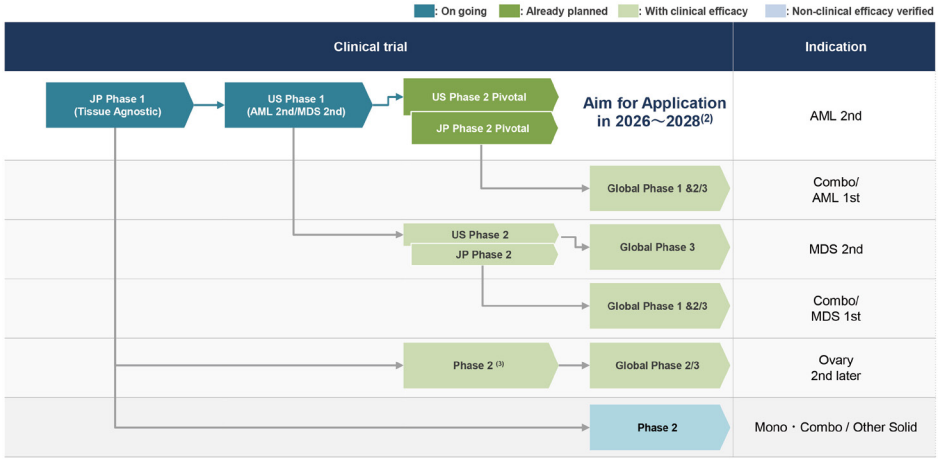
Guided by its aspiration to develop and deliver groundbreaking new anti-cancer drugs from Japan to patients as soon as possible, the Company is working towards its vision for 2030 to be an R&D-oriented pharmaceutical company based in Japan. Its strategy is to efficiently expand business by handling manufacturing and sales in-house through strategic alliances in Japan and concluding license agreements with global pharmaceutical companies in overseas markets.

Turning to development strategy, the Company's goal for the foreseeable future is to achieve monetization early on by concentrating management resources on CTX-712, working first to obtain marketing approval in the US and Japan for relapsed and refractory lymphomas, and then striving to maximize CTX-712's product value by pursuing expansion of indications to first-line treatment for AML, other types of cancer, and so forth. As previously mentioned, the potential market scale is large and CTX-712 has the potential to become a blockbuster, so focus will be on the content of the interim results from the Phase 1 part of the clinical trial expected to be released around the end of 2025. FISCO believes the possibility of concluding license agreements overseas will rapidly rise if favorable results are obtained. If CTX-712 subsequently proceeds smoothly into the Phase 2 part of the clinical trial and obtains the expected results* for the CR rate, which is the primary endpoint, the Company expects to be able to submit an NDA in the first half of 2027 and book revenue in FY8/28. In addition, it may be able to receive around the same time a second milestone payment from progress developing the MALT1 inhibitor out-licensed to Ono Pharmaceutical. If those things happen, a turn to profit for the single fiscal year would also come into sight.

* Syndax Pharmaceuticals' Revumenib, which is considered likely to receive marketing approval in the US for the treatment of AML, had a CR rate of 18% in a Pivotal P2 study. Therefore, Chordia Therapeutics believes approval is likely if the CR rate is about 20% or higher (CR rate was 29% in the Phase 1 study conducted in Japan).

Results trends

Development strategy



Source: The Company's results briefing materials

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