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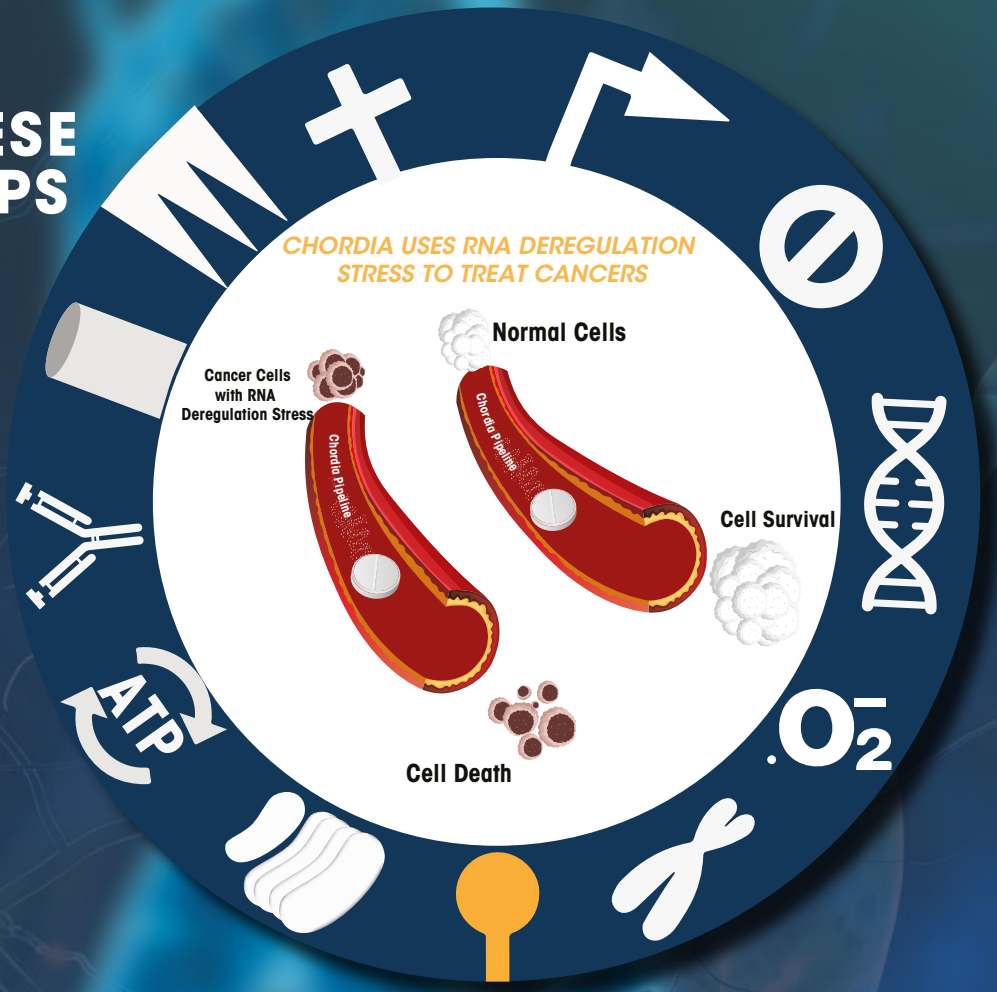

RNA DEREGULATION STRESS, NEW HALLMARKS OF CANCER

CHORDIA THERAPEUTICS INC.

A Better Tomorrow Through Innovative Therapy

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WE AIM TO DEVELOP LIFE-CHANGING TREATMENTS FOR CANCER BY GENERATING SMALL-MOLECULE MEDICINES THAT PREVENT OR MODIFY RNA DEREGULATION

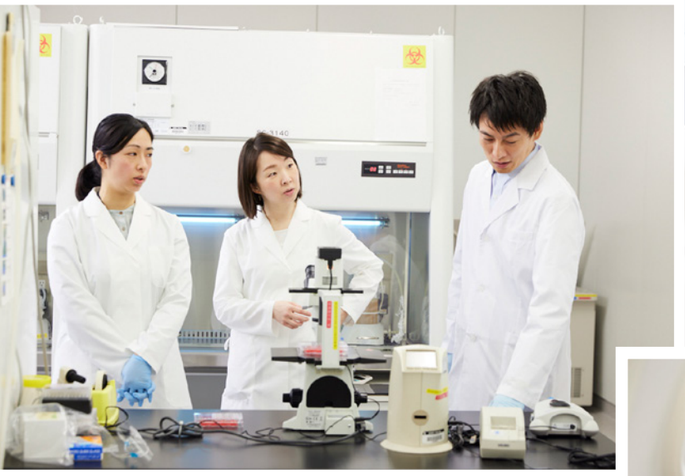
Dr. Daisuke Morishita,
CTO of Chordia Therapeutics

CHORDIA THERAPEUTICS INC.

A Better Tomorrow Through Innovative Therapy

Two decades ago, Douglas Hanahan and Robert Weinberg published their influential review: The Hallmarks of Cancer–a study that proved to be groundbreaking in understanding cancer's common traits and the rational design and manufacturing of drugs. This review organized the complexities of cancer into six major hallmarks: self-sufficiency in growth signals, insensitivity to anti-growth signals, evading apoptosis, limitless replicative potential, sustained angiogenesis, and tissue invasion and metastasis. In addition to these original six hallmarks, scientists have since identified equally prevalent hallmarks, referred to as stress phenotypes of cancer. Although these cancer phenotypes are not responsible for initiating tumorigenesis, they are common characteristics across several types of tumors. Now, a novel hallmark of cancer, RNA deregulation, has been newly proposed as another indication of cancer within this group of stress phenotypes. However, exploiting and leveraging RNA deregulation in cancer therapy is uncharted territory for most drug manufacturers and pharmaceuticals. Chordia Therapeutics aims to bring this technology into the limelight.

Driven by science and new-age research in developing the next generation of small-molecule inhibitors for cancer treatment, Chordia Therapeutics is a Japanese startup that has developed drugs that



overload RNA deregulation stress by changing RNA splicing to initiate the death of cancer cells. The company's innovations are powered by the experience of its highly skilled team that is constantly developing First-in-Class small-molecule anticancer drugs with modern mechanisms of action.

RNA DEREGULATION–A NOVEL STRATEGY FOR CANCER THERAPY

"We aim to develop life-changing treatments for cancer by generating small-molecule medicines that prevent or modify RNA deregulation," says Dr. Daisuke Morishita, CSO of Chordia Therapeutics. RNA stress is caused by gene mutations of proteins and the abnormality of molecules and nucleic acid sequences brought about by enzyme inactivity. The Chordia pipeline is built on the team's expertise in RNA deregulation.

The team is developing pipelines that target splicing (CLK inhibitors), transcription (CDK12 inhibitors), tRNA recruitment (GCN2 inhibitors), RNA degradation (undisclosed information) and generate aberrant RNA that creates additional stress in cancer cells. Additionally, Chordia collaborates with academic researchers to analyze innovative next-generation sequencing and gene-editing systems. Proactive research allows the team to thoroughly understand neoplastic disease states involving RNA deregulation, expediently drive the discovery of new therapeutic targets, and better define patient selection strategies.

DRUGS THAT INDIRECTLY ELIMINATE CANCER CELLS

Currently, no FDA-approved drugs inhibit transcription, splicing, degradation, or tRNA recruitment, allowing Chordia's assets to become first-in-class drugs. First-in-class drug discovery may prove to be highly effective in patients who have not responded to previous therapies and help pharma organizations massively increase their revenue since it is the only drug of its kind on the market.

Chordia's first-in-class drug, CTX-712, targets cancer cells with a splicing factor (SF) mutation; this drug kills cancer cells when they exhibit splicing vulnerability as a CLK inhibitor. CTX-712 dephosphorylates serine and arginine-rich (SR) proteins and induces, primarily, skipped exon types of splicing changes which generate RNA deregulation stress. "Although CTX-712 has proven to be efficacious against a wide range of cancers in non-clinical studies, we found that CTX-712 selectively induces cell death, particularly for cancers with genetic mutations in Splicing factors," says Dr. Morishita. It is an orally available, selective, small-molecule inhibitor of CDC-like kinase (CLK). CTX-712 inhibits RNA splicing to generate RNA deregulation stress, which causes cancer cell death and tumor growth inhibition in multiple preclinical models. In its preclinical research trials, CTX-712 demonstrated prowess against a wide variety of cancer cells and exhibited a good safety profile. The drug is now in its Phase 1 trial, conducted at several research centers, including the National Cancer Center Hospital in Japan, and has commenced a new chapter in cancer therapy development as it is one of the first therapies to explore the targeting of RNA deregulation stress.

Chordia Therapeutics also engaged in a licensing agreement for preclinical asset CTX-177, a selective small-molecule inhibitor of mucosa associated lymphoid tissue lymphoma translocation protein 1 (MALT1), with Ono Pharmaceutical in December 2020. Ono Pharmaceutical is the developer of Opdivo and is a leading global oncology player, and the organization's interest in Chordia's drug development is a testament to the high value of Chordia's assets. The contract will fund the company JPY 3.3 billion at the start of CTX-177's Phase 1 clinical trial, JPY 49.6 billion if subsequent certain development and commercial milestones are achieved.

Additional compounds in preclinical development include CTX-439—a first-in-class inhibitor of cyclin-dependent kinase 12 (CDK12)—and CRD-1968099, which inhibits general control nonderepressible 2 (GCN2). These orally available compounds increase RNA deregulation stress by interfering with RNA transcription and tRNA recruitment, respectively, and have shown anticancer effects in preclinical models as a single reagent, as well as in a combination therapy with other medications. Chordia is proceeding with these preclinical pipelines and will soon begin clinical trials.

WE ARE ADVANCING DRUG DEVELOPMENT QUICKLY AND STEADILY BY MAKING THE BEST USE OF THE FLEXIBILITY OF A LEAN ORGANIZATION, A BROAD NETWORK OF EXPERIENCED PROFESSIONALS, AND OUR ACCUMULATED R&D WISDOM

A COMPANY BACKED BY DECADES OF PHARMA RESEARCH

Branching out from Takeda Pharmaceutical in November 2017, Chordia Therapeutics has quickly matured into a clinical-stage biotech company engaged in researching and developing novel therapies for cancers with high unmet medical needs. "In order to develop next-generation anticancer drugs based on definite scientific evidence, we focused on RNA control abnormalities found as new features of cancer and obtained exclusive licensing rights from Takeda for four non-clinical anticancer drug candidate programs," says Dr. Hiroshi Miyake, CEO of Chordia, and Site Head of Oncology Research for Japan at Takeda Pharmaceutical. Dr. Morishita also spent a decade at Takeda Pharmaceutical, working on oncology therapeutic areas, especially in cancer-related RNA networks. During his ten years as the representative of industry-academia collaboration programs in Takeda, Dr. Morishita took the lead in the drug discovery research of CTX-177. He then translated and passed his knowledge onto the teams at Chordia to continue this research.

Chordia's expertise as an innovative drug manufacturer stems from its dedication to swift R&D derived from quick decision-making and gratitude to its external partners who support the company. "We are advancing drug development quickly and steadily by making the best use of the flexibility of a lean organization, a broad network of experienced professionals, and our accumulated R&D wisdom," adds Dr. Miyake.

A VISION FOR A BRIGHT FUTURE IN ONCOLOGY

As the development of genetic analysis technology and its application in medical treatment advances, experts anticipate that drug manufacturers and healthcare practitioners will focus on previously overlooked patient groups and diseases. Compounding the knowledge gleaned from these studies, organizations can thoroughly analyze the relationship between gene mutations of patients and their symptoms and will, in turn, optimize therapies. Chordia Therapeutics is already several steps ahead of contemporary organizations since the team not only foresees this trend but has also taken steps to actualize it with their out-of-the-box research on RNA deregulation. Furthermore, to realize personalized medicine, Chordia strives to create efficient R&D processes in collaboration with stakeholders in various fields including universities, other companies, hospitals, and investors. Staying true to the company's name (derived from the word 'chord,' which signifies a pleasant sound when musical notes are played synchronously), Chordia is harmonizing their energy and passion for science with collaborators, supporters, and stakeholders to enable the discovery of innovative drugs.