Court File No. T- 984 -20

FEDERAL COURT

B E T W E E N:

CATALYST PHARMACEUTICALS, INC.
and KYE PHARMACEUTICALS INC.

Applicants

- and -

ATTORNEY GENERAL OF CANADA,
THE MINISTER OF HEALTH
and MÉDUNIK CANADA

Respondents

NOTICE OF APPLICATION

TO THE RESPONDENTS

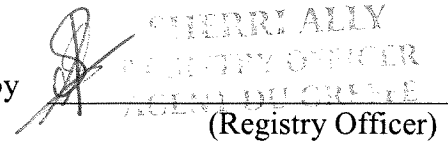
A PROCEEDING HAS BEEN COMMENCED by the applicants. The relief claimed by the applicants appears on the following pages.

THIS APPLICATION will be heard by the Court at a time and place to be fixed by the Judicial Administrator. Unless the Court orders otherwise, the place of hearing will be as requested by the applicants. The applicants request that this application be heard at Toronto, Ontario.

IF YOU WISH TO OPPOSE THIS APPLICATION, to receive notice of any step in the application or to be served with any documents in the application, you or a solicitor acting for you must file a notice of appearance in Form 305 prescribed by the *Federal Courts Rules* and serve it on the applicants' solicitor or, if the applicants are self-represented, on the applicants, WITHIN 10 DAYS after being served with this notice of application.

Copies of the *Federal Courts Rules*, information concerning the local offices of the Court and other necessary information may be obtained on request to the Administrator of this Court at Ottawa (telephone 613-992-4238) or at any local office.

IF YOU FAIL TO OPPOSE THIS APPLICATION, JUDGMENT MAY BE GIVEN IN YOUR ABSENCE AND WITHOUT FURTHER NOTICE TO YOU.

Date August 26, 2020 Issued by  (Registry Officer)

Address of local office: 180 Queen Street West
Suite 200
Toronto, Ontario
M5V 3L6

TO: **Attorney General of Canada**
Department of Justice
Ontario Regional Office
120 Adelaide Street West
Suite 4000
Toronto, ON M5H 1T1
Email: Tor.leadadmissions@justice.gc.ca

(service to be effected by filing duplicate copies in the Registry pursuant to Rule 133 and Section 48 of the *Federal Courts Act*)

(service to be effected by email further to Notice re Service on the Crown at https://www.justice.gc.ca/eng/contact/Comm3.html)

AND TO: **The Minister of Health**
Office of Submissions and Intellectual Property
Office of Patented Medicines and Liaison
Finance Building
101 Tunney's Pasture Driveway
Ottawa ON K1A 0K9

(service to be effected by filing duplicate copies in the Registry pursuant to Rule 133 and Section 48 of the *Federal Courts Act*)

AND TO: **Médunik Canada**
950 Boulevard Michèle-Bohec
Blainville, QC J7C 5E2

APPLICATION

THIS IS AN APPLICATION for judicial review of the decision of the Minister of Health ("Minister"), made on or about August 10, 2020, wherein the Minister issued to Médunik Canada ("Médunik") a Notice of Compliance ("NOC") in respect of Médunik's New Drug Submission ("NDS") for its Ruzurgi™ 10 mg tablets, contrary to s. 3(b) of section C.08.004.1 of the *Food and Drug Regulations*, CRC, c. 870 (the "Decision").

THE APPLICANTS MAKE APPLICATION FOR:

(a) an order quashing the Decision and the NOC issued to Médunik;

(b) an order prohibiting the Minister from issuing a NOC to Médunik in respect of its Ruzurgi™ product until August 1, 2028 (eight years after the date of issuance of Catalyst Pharmaceutical Inc.'s ("Catalyst") NOC for its amifampridine phosphate product, Firdapse®);

(c) in the alternative to (b), an order referring the matter back to the Minister for redetermination in accordance with s. 3(b) of section C.08.004.1 of the *Food and Drug Regulations* and such other directions as this Court considers appropriate;

(d) an expedited hearing and schedule of this application;

(e) an interim order under s. 18.2 of the *Federal Courts Act*, including staying the effect of the grant of the NOC to Médunik for its Ruzurgi™, pending final determination of this application;

(f) an order granting the Applicants their costs of this application; and

(g) such further and other relief as to this Honourable Court may seem just.

THE GROUNDS FOR THE APPLICATION ARE:

The Applicants

1. Catalyst is a Florida-based biopharmaceutical company focused on investing in the development and commercialization of innovative therapies for those who suffer from rare and ultra-rare diseases. Catalyst's mission is to improve the lives of patients with these rare and debilitating conditions, who often have no therapeutic options.

2. Kye Pharmaceuticals Inc. ("Kye") is a Canadian pharmaceutical company founded in 2019 dedicated to bringing medicines to the Canadian market that fulfill clinically significant and unmet needs.

3. Catalyst and Kye have entered into an exclusive license agreement whereby Kye will commercialize Catalyst's amifampridine phosphate product, Firdapse®, in Canada. Kye has filed an administrative NDS, with Catalyst's consent, that once approved, will grant marketing authorization to Kye for Firdapse® in Canada.

The Respondent Médunik

4. The respondent Médunik is a manufacturer or supplier of pharmaceutical products with an address located in Blainville, QC. It is the sponsor of the NDS bearing submission control number 234655 in respect of its amifampridine product, Ruzurgi™.

Amifampridine and LEMS

5. Lambert-Eaton myasthenic syndrome ("LEMS"), a debilitating neuromuscular syndrome, is an autoimmune disorder where the immune system attacks the neuromuscular junction (the "NMJ", which is the connection between nerves and muscles), interfering with the ability of nerve cells to send signals to muscle cells. LEMS generally affects the extremities, causing muscle weakness, especially in the legs and hips, which can ultimately lead to difficulty walking. Weakness in the eye muscles and those involved in talking, swallowing and chewing

may also occur. LEMS may also be associated with small-cell lung cancer, where its onset precedes or coincides with the cancer diagnosis.

6. LEMS is a rare disease. It is estimated to affect 3-4 of every 1 million individuals worldwide and can occur at any age. Approximately 200 Canadians suffer from LEMS. The number of newly diagnosed LEMS patients is much smaller.

7. Amifampridine phosphate, the active ingredient in Catalyst's Firdapse® product, treats LEMS by increasing the amount of a particular neurotransmitter, acetylcholine (ACh), in the NMJ so that ACh can improve muscle function. Specifically, Firdapse works by blocking the potassium channel in the nerve cell, which keeps calcium channels open longer, allowing more ACh to be released into the NMJ.

Catalyst's development of Firdapse® (amifampridine phosphate)

8. Firdapse® is known as an "orphan drug" – one which pharmaceutical companies are reluctant to develop under usual marketing conditions because the small market does not allow the recovery of the capital invested for its research. Although amifampridine was first discovered in Scotland in the 1970s, before the approval of Firdapse®, amifampridine was not commercially available. It was only available to a small group of patients under special access programs in limited jurisdictions.

9. Catalyst expended considerable time, effort and resources to obtain regulatory approval for Firdapse®. It sponsored two phase 3 clinical trials to support the approval of amifampridine phosphate in the treatment of LEMS. Phase 3 trials are the last step before a new drug can be submitted for regulatory approval. Because of their size and comparatively long duration, phase 3 trials are usually the most expensive, time-consuming and difficult clinical trials to design and run. Both randomized trials of Firdapse® resulted in positive, statistically significant data and in 2018 Catalyst filed a New Drug Application ("NDA") with the United States Food and Drug Administration (FDA) for amifampridine phosphate for the treatment of LEMS.

10. In order to obtain regulatory approval for Firdapse®, Catalyst was also required to provide extensive non-clinical safety and toxicology testing to the regulatory authorities. This included a study of the potential impact of amifampridine phosphate on fertility in animals (the "Impairment of Fertility Study") and an animal carcinogenicity study (the "Carcinogenicity Study"). Catalyst sponsored (i.e., paid for) each of these studies in order to be able to substantiate its product's safety.

11. The NDA for Firdapse® was granted Priority Review and Breakthrough Therapy designations, which are FDA processes designed to dedicate additional resources to and expedite review of important and potentially ground-breaking therapies. Firdapse® also received an Orphan Drug designation, an FDA program which provides incentives to assist and encourage the development of drugs for rare diseases.

12. There is no special review framework dedicated to orphan drugs in Canada. However, there are fast-tracked pathways available to manufacturers if a drug is intended for the treatment, prevention or diagnosis of serious, life-threatening or severely debilitating diseases or conditions and there is no alternative therapy available on the Canadian market. One such pathway is "Priority Review" status, which shortens the normal 300-day Health Canada review process to 180-days. In its regulatory submission for Firdapse® in Canada, described further below, Catalyst was granted Priority Review status.

The data protection regime in Canada

13. In Canada, new drugs may be entitled to data protection. In 2006, Canada amended the data protection provisions of the *Food and Drug Regulations* to provide the manufacturer of an "innovative drug" with an internationally competitive, guaranteed minimum period of market exclusivity.

14. The amendments were intended to clarify and effectively implement Canada's obligations under the North American Free Trade Agreement and the Agreement on Trade-Related Aspects of Intellectual Property Rights. The introduction of this

market exclusivity was intended to provide an adequate incentive for innovators to invest in research, and to develop and market their products in Canada.

15. The data protection provisions of the *Food and Drug Regulations* are found in section C.08.004.1 (the "data protection regulations"). The heart of the data protection regulations is section 3, which sets out two time periods that protect an innovator drug from competition from a manufacturer seeking a notice of compliance on the basis of a direct or indirect comparison to the innovator drug: a "no file" period of six years and a "data protection" or "market exclusivity" period of eight years. In particular, section 3 provides that "[i]f a manufacturer seeks a notice of compliance for a new drug on the basis of a direct or indirect comparison between the new drug and an innovative drug,

> (a) the manufacturer may not file a new drug submission, a supplement to a new drug submission, an abbreviated new drug submission or a supplement to an abbreviated new drug submission in respect of the new drug before the end of a period of six years after the day on which the first notice of compliance was issued to the innovator in respect of the innovative drug; and
>
> (b) the Minister **shall not approve that submission or supplement and shall not issue a notice of compliance in respect of the new drug before the end of a period of eight years after the day on which the first notice of compliance was issued to the innovator in respect of the innovative drug** [emphasis added].

16. The effect of the "market exclusivity" period set out in section 3(b) is that a manufacturer of an "innovative drug" is protected from unfair commercial use of its safety and efficacy data by other manufacturers for eight years after the innovative drug receives its NOC.

Catalyst received data protection for Firdapse®

17. Catalyst filed its NDS for Firdapse® with Health Canada on October 18, 2019. Health Canada granted Firdapse® "Priority Review" status on September 13, 2019.

18. In order to protect its investment in this breakthrough drug in the Canadian marketplace, Catalyst sought data protection for Firdapse®, asking the Minister to classify it as an "innovative drug" under the data protection regulations.

19. By letter dated November 19, 2019, the Minister advised Catalyst that Firdapse® appeared to be an "innovative drug" and was therefore eligible for data protection. It further stated that, subject to a final review at the time the submission would receive a NOC, Firdapse® would be added to the Register of Innovative Drugs for a term of eight years from the date of the issuance of the NOC.

20. Catalyst was issued a NOC for Firdapse® on July 31, 2020. It was also granted data protection commencing on that date. Firdapse® was subsequently added to the Register of Innovative Drugs.

21. As a result of receiving data protection, Firdapse® benefits from the six-year "no file" period, and the eight-year "data protection" or "market exclusivity" period from the date of its NOC. Catalyst was therefore supposed to receive market exclusivity in respect of Firdapse®, to reward its investment in the research required to develop and market Firdapse® in Canada.

22. Each of the Carcinogenicity Study and the Impairment of Fertility Study referred to above were essential for the regulatory approval of amifampridine phosphate and to describe its safety profile. Indeed, a minimum of one carcinogenicity study was required for approval. In the product monograph for Firdapse® the Carcinogenicity Study is not only included in the Non-clinical Data section but also in the Warnings and Precautions section to further characterize the clinical safety profile of the drug. Both the Carcinogenicity Study and Impairment of Fertility Study are therefore included within the "data" protected by the data protection regulations.

Médunik's amifampridine product (Rugurzi™)

23. In December 2019, after Firdapse had received a preliminary notice from OPML that Firdapse® would be designated an "innovative drug" and would benefit

from data protection, Médunik filed a NDS for its amifampridine product, Ruzurgi™. Ruzurgi™ is a free base form of amifampridine (in contrast to Firdapse®, which is a phosphate salt).

Médunik's Ruzurgi™ submission is based on a comparison to Firdapse®

24. In filing its submission for Ruzurgi™, Médunik did not do its own Carcinogenicity Study or its own Impairment of Fertility Study. Instead, it relied on Catalyst's data that had been generated in respect of Firdapse®. In other words, in seeking a notice of compliance for its amifampridine product, Médunik's submission was based on a comparison between Ruzurgi™ and Firdapse®.

25. Specifically, in the "Non-Clinical Toxicology" section of the Ruzurgi™ product monograph (as approved by Health Canada), Médunik explains that "Carcinogenicity studies of RUZURGI (amifampridine) have not been conducted." Instead, Médunik relies on Catalyst's Carcinogenicity Study. Similarly, Médunik explains that "Animal studies to assess the potential adverse effects of RUZURGI (amifampridine) on fertility and embryofetal development have not been conducted." Médunik therefore also relies on Catalyst's Impairment of Fertility Study. Médunik's NDS thus explicitly relied on studies that had been conducted by Catalyst to establish the safety and tolerability of Firdapse®. Moreover, without relying on data obtained by Catalyst in developing Firdapse®, Ruzurgi™ would not have met Health Canada's safety and tolerability requirements and would not have obtained a NOC.

26. Thus, in seeking approval for Ruzurgi™, Médunik's submission was based on a direct, or at the very least an indirect, comparison between its amifampridine product and Firdapse®.

27. Moreover, as explained above, at the time the Minister decided to approve Ruzurgi™, Firdapse® was an "innovative drug" under the data protection regulations.

The Minister's decision to overlook Firdapse®'s data protection

28. On or about August 10, 2020 – ten days after Firdapse® received its NOC and was granted data protection – the Minister issued a NOC to Médunik for its Ruzurgi™ product.

29. Since Médunik had compared Ruzurgi™ to Firdapse® in seeking its NOC for Ruzurgi™, section 3(b) of the data protection regulations prohibited the Minister from:

(a) approving Médunik's submission for Ruzurgi™; and

(b) issuing a NOC to Ruzurgi™

before the end of a period of eight years after the day on which Catalyst received its NOC for Firdapse®, the innovative drug, namely, July 31, 2028.

30. The Minister's decision to issue a NOC to Médunik was therefore both incorrect and unreasonable. At the time the Minister decided to approve and grant a NOC to Ruzurgi™, Catalyst had already been granted its NOC for Firdapse®, and it had been designated an "innovative drug" under the data protection regulations. Firdapse® was therefore entitled to data protection. Subsection 3(b) of the data protection regulations should have prevented the Minister from issuing a NOC to Médunik for eight years from the date of Catalyst's NOC (because in the Ruzurgi™ submission, Médunik was seeking a NOC for a new drug on the basis or a direct or indirect comparison between Ruzurgi™ and Firdapse®).

31. Furthermore, to the extent that the Minister had any doubt about the application of Firdapse®'s data protection to Ruzurgi™'s approval under section 3(b) of the data protection regulations, Catalyst should have been given notice of the Minister's decision to overlook or otherwise ignore Firdapse®'s data protection and been given the opportunity to respond. It was given neither. Instead, Catalyst was surprised to find out, after the fact, that even though Firdapse® had received data protection, Médunik had nevertheless received a NOC for Ruzurgi™, contrary to

section 3(b) of the data protection regulations. The Applicants have therefore been denied the right to procedural fairness.

Rule 317 request

32. The Applicants request the Minister to send, taking appropriate steps to maintain confidentiality, a certified copy of the following material that is not in the possession of the Applicants but is in the possession of the Minister, to the Applicants and to the Registry:

(a) all material considered and created by the Minister, including all internal documentation and communications pertaining, or relevant, to the Minister's Decision as defined herein.

Hearing of this application

33. The Applicants are seeking an expedited hearing of this application, to be heard in December 2020, or earlier if possible.

34. The mode of the hearing of this application shall be determined by the Court.

Statutes and regulations relied on

35. Section C.08.004.1 of the *Food and Drug Regulations*.

36. Sections 18.1 and 18.2 of the *Federal Courts Act*, R.S.C. 1985, c. F-7.

37. Rules 3, 8, 317 and 318 of the *Federal Courts Rules*.

38. Such other grounds as counsel may advise and this Honourable Court may permit.

THIS APPLICATION WILL BE SUPPORTED BY THE FOLLOWING MATERIALS:

(a) The affidavits of one or more individuals; and

(b) Such further and other materials as counsel may advise and this Honourable Court permit.

August 26, 2020

Torys LLP
79 Wellington St. W., 30th Floor
Box 270, TD South Tower
Toronto, ON M5K 1N2
Fax: 416.865.7380

Andrew Shaughnessy
Tel: 416.865.8171
ashaugnessy@torys.com

Yael Bienenstock
Tel: 416.865.7954
ybienenstock@torys.com

Alexandra Peterson
Tel: 416.865.8114
apeterson@torys.com

Solicitors for the Applicants