

UNITED STATES PATENT AND TRADEMARK OFFICE

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BEFORE THE PATENT TRIAL AND APPEAL BOARD

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MURRAY & POOLE ENTERPRISES, LTD.,

Petitioner,

v.

INSTITUT DE CARDIOLOGIE DE MONTREAL,

Patent Owner,

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Case IPR2023-01064

Patent No. 11,400,063

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**DECLARATION OF JEAN-CLAUDE TARDIF, M.D.**

1. I, Jean-Claude Tardif, M.D., submit this declaration in the above-referenced proceeding in support of the Patent Owner's Preliminary Response to the Petition filed in this matter.

2. I am the named inventor on U.S. patent No. 11,400,063 ("the '063 patent"), which is the patent that is at issue in the Petition. (EX1001.) As stated in my affidavit to the United States Patent Office during prosecution of the '063 patent, I am the sole inventor of the '063 patent.

3. I am not being separately compensated for my work preparing this declaration, but I am a full time employee of Patent Owner, Institut de Cardiologie de Montreal, which I will refer to as the "Montreal Heart Institute" or "MHI."

4. I have personal knowledge of everything set forth in this declaration unless specifically noted otherwise.

5. The Bouabdallaoui reference—EX1005 and a reference on which I am a co-author—is a publication of my invention, or substantively the same subject matter of my invention by me with others who obtained the subject matter disclosed therein directly or indirectly from me. The Bouabdallaoui reference was provided to the Examiner during prosecution of the '063 patent and there was no effort to conceal the reference from the Examiner because the reference described my work and was published less than one year before the filing of the application that issued as the '063 patent.

## **I. PERSONAL BACKGROUND**

6. I am currently the Director of the Research Center at MHI and Professor of Medicine at the University of Montreal.
7. I received my medical degree (MD) in 1987 from the University of Montreal, where I specialized in cardiology and research.
8. I hold the Canada Research Chair in personalized medicine and the University of Montreal endowed research chair in atherosclerosis. I am also the Scientific Director of the Montreal Health Innovations Coordinating Center (MHICC).
9. Along with my team, I created the Beaulieu-Saucier Pharmacogenomics Center at the Montreal Heart Institute and the Center of Excellence in Personalized Medicine, the latter funded by the Network of Centers of Excellence of Canada and which has also been supported by multiple pharmaceutical and biotechnological companies.
10. I have won multiple awards, including the Research Achievement Award of the Canadian Cardiovascular Society, the Distinguished Lecturer Award of the Canadian Institutes for Health Research, the Genesis Award of BIOQuébec (for outstanding contributions to life sciences), the Armand-Frappier Award of the Government of Québec (the highest scientific honour in Quebec) and the Margolese National Heart Disorders Prize (for outstanding contributions to the

treatment, amelioration, or cure of heart disorders). Because of my accomplishments, I was named Fellow of the Canadian Academy of Health Sciences and Fellow of the Royal Society of Canada and was inducted in the Order of Canada (the highest distinction in the country).

11. I have authored more than 750 scientific articles on a variety of issues with a particular focus on cardiovascular disease. My research covers the molecular and genomic aspects of atherosclerosis and related diseases and also involves animal models, mechanistic and observational clinical studies as well as early clinical trials and large international randomized clinical trials.

12. I have served as the international principal investigator or part of the study leadership of several large clinical trials in the field of atherosclerosis and other cardiovascular diseases. In addition to serving as the principal investigator for clinical studies, I have also designed clinical studies including the Colchicine Cardiovascular Outcomes Trial (“COLCOT”) study.

## **II. COLCHICINE, CARDIOVASCULAR PATIENTS, AND THE COLCOT CLINICAL STUDY.**

13. Colchicine is an anti-inflammatory medication that was originally indicated for the treatment of gout, familial Mediterranean fever, and pericarditis.

14. Because of colchicine’s anti-inflammatory properties and its use in treating pericarditis, industry professionals, including myself, began to investigate the use of colchicine in treating patients that had experienced cardiovascular

events.

15. In 2013, Nidorf et al. published an article describing the Low-Dose Colchicine (LoDoCo) clinical study that dosed patients with stable coronary disease with 0.5 mg doses of colchicine. (EX1001, the '063 Patent, at 1:52-59.) The LoDoCo study was a small scale study (only 532 patients) that was not placebo controlled, and from which it was therefore difficult to draw meaningful clinical conclusions. (*Id.*)

16. To overcome the deficiencies of the LoDoCo study, I designed the COLCOT study. My goal with COLCOT was to conduct a large-scale, international, placebo-controlled study to evaluate the effects of low dose colchicine on cardiovascular outcomes as well as to determine the long-term safety profile in patients who recently had experienced myocardial infarction. The intended patient population was patients who had experienced a recent myocardial infarction (within 30 days) and all patients would have had completed a percutaneous coronary intervention if indicated. The primary endpoint for the study was a composite of cardiovascular death, resuscitated cardiac arrest, myocardial infarction, stroke, or urgent hospitalization for angina requiring coronary revascularization. The study also provided for three different cutoffs for time-to-treatment initiation of colchicine to determine the association between early initiation of colchicine therapy and clinical outcomes. Specifically, the trial

looked at intervention initiated between day 0 to 3, from day 4 to 7, and from day 8 to 30.

17. I personally conceived of and designed the COLCOT study and its protocol. In preparing the protocol for the study, I received input from colleagues at MHI, but the study and its protocol were my conception and responsibility. I also obtained the funding to conduct the COLCOT study. (EX2016.)

18. In addition, I was the principal investigator for the COLCOT study. This is verified by page 6 of EX1006, which I understand is a copy of a description of the COLCOT study and protocol obtained from ClinicalTrials.gov. The principal investigator is not an honorary title but instead is the lead investigator that is responsible for supervising the funding and conduct of the clinical trial, and for facilitating communications with funding organizations and regulatory authorities regarding the outcome of the trial. In the U.S. clinical trial registry, my facility, MHI, is listed as the responsible party and location for the study as well as the repository from which all information on the study was provided to the government. (EX1006 at p. 6.)

19. Often, as was the case here, it is impractical for a single clinician to alone enroll enough patients to fill a large-scale clinical study. It is common for a principal investigator to use clinicians at other hospitals or clinics to participate in a study, obtain results from patients that are included in the study, and to pool

those results in order to create more robust data. In order to conduct the COLCOT study at the magnitude that was necessary to determine whether any clinical outcomes were meaningful, I personally recruited investigators from 167 different facilities including MHI. These were investigators and clinics with which MHI and I personally had previous professional relationships. We entered into agreements with these investigators, examples of which are found at EX2012 - 2015, to conduct the COLCOT study according to the protocol that I designed and provided to the investigators. These agreements show that the investigators were part of the multi-site study, and that MHI had overall supervision and responsibility for the COLCOT study. (EX2012 at 3-5, 9-10; EX2013 at 9-12, 14-15; EX2014 at 6-7, 10-12; EX2015 at 6-8, 12-13.) Each site agreed that any results from the clinical study were confidential, were to be provided to MHI, and were intellectual property that was owned by MHI. (EX2012 at §§5, 7, 8; EX2013 at §§5, 7, 8; EX2014 at §§5, 7, 8; EX2015 at §§5, 7, 8.) Further, the investigators understood that MHI had the right of first publication, and that they were not permitted to publish any data without the prior approval of MHI. (EX2012 at §7; EX2013 at §§7,8; EX2014 at §7; EX2015 at §7.)

20. Across all clinics, the COLCOT study enrolled 4,745 patients for both the active arm and the placebo-controlled group. The study began in mid-2015 and the data was collected and analyzed in 2019 and 2020. Data from all of the clinical

sites was provided to me from all clinical sites. I then instructed Marie-Claude Guertin, a statistician employed by MHICC with whom I had worked in the past, to perform a data analysis at my direction and to report the results to me.

21. As reported in the '063 patent, the COLCOT study showed that patients who had experienced myocardial infarction had a reduced risk of the primary efficacy endpoint when administered a low dose of colchicine within 30 days of the myocardial infarction. In addition, the COLCOT study showed that for certain patients who had suffered a myocardial infarction, administration of a low dose of colchicine within 3 days of the myocardial infarction had several benefits, including a reduced risk of cardiovascular events, without the need of a pre-loading higher dose of colchicine. These results were surprising and not previously reported in the industry, and offered a tremendous opportunity for patients who experienced a myocardial infarction.

### **III. PATENTS AND PUBLICATIONS RELATING TO COLCOT STUDY**

22. In November 2019, U.S. provisional patent application No. 62/935,865 which included information relating to the COLCOT study was filed listing me as the sole inventor. (EX1001, cover.) I authored an article describing the COLCOT study and certain results from the study that was published in the December 2019 edition of the New England Journal of Medicine titled “Efficacy and Safety of Low-Dose Colchicine after Myocardial Infarction,” (“Tardif”).

(EX1022.) I caused provisional application No. 63/093,988 to be filed on October 20, 2020. (EX1001, cover.) On November 13, 2020, I caused U.S. Patent application no. 17/097,285 (“the ’285 application”) to be filed, which I have been informed claims priority to the provisional applications. (*Id.*)

23. During prosecution of the ’285 application, I provided an affidavit stating that I am the inventor of the invention described in the application. (EX1002 at 338.) That statement was true at the time that I made it and remains true today. Also, during prosecution of the ’285 application, I instructed attorneys prosecuting the ’285 application to provide copies of the Tardif article and the Bouabdallaoui article to the patent Examiner. (EX1002 at 75-77.)

24. On August 2, 2022, having been provided the Bouabdallaoui article, the Examiner issued the ’063 patent from the ’285 application.

25. The Bouabdallaoui article relates to the COLCOT clinical study and its results. While the Tardif article focused more on the initial results of COLCOT, the Bouabdallaoui article focuses more on the results of the study that relate to early intervention with colchicine.

26. The Bouabdallaoui article lists that it was published online August 29, 2020, which is 9 months after the first provisional application that I filed and 2 months and 3 months after the filing dates of the second provisional application and the ’285 application, respectively.

27. I am not the first named author of Bouabdallaoui, but that is immaterial. As seen from EX1005, I am listed on the first page of the article as the corresponding author. Those in the industry understand that the corresponding author is the individual responsible for the article and getting it into publication, and speaks on behalf of the other co-authors with respect to the article. The corresponding author is responsible for, among other things, manuscript corrections, copyright and publishing agreements, and responding to inquiries about the article on behalf of the co-authors.

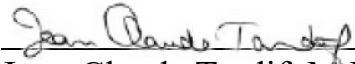
28. I was the primary author of the Bouabdallaoui article. The article itself is based on a clinical study that I designed, developed, and served as the principal investigator on. The data generated from the clinical study that was included in Bouabdallaoui was collected, provided to me, and was analyzed at my direction. The co-authors on Bouabdallaoui were provided information about the COLCOT study results from me. As seen from the agreements with the investigators, MHI was provided data from the COLCOT study from all the individual study sites, and that data was the property of MHI. (EX2012 at §8; EX2013 at §8; EX2014 at §8; EX2015 at §8.) MHI had the first publication rights to all that data and was able to prohibit or delay publication of any data by any individual site. (EX2012 at §7; EX2013 at §7; EX2014 at §7; EX2015 at §7.) The agreements also provided for joint publications among the sites, and I coordinated

revisions of and communications regarding drafts of the article by my co-authors. However, I had final say on the contents of the article.

29. I included the co-authors to acknowledge their assistance and work in obtaining and collecting the data for the COLCOT study. In fact, at the time Dr. Bouabdallaoui was relatively early in her career and I had her listed as the first author on the publication to acknowledge her assistance in conducting the trial as well as to provide a “first author” publication for her CV. However, as the basis of the '063 patent, the COLCOT study was my design and related to my initial hypotheses regarding the use of colchicine for treating cardiovascular patients. The co-authors of Bouabdallaoui had the complete information regarding the results of the COLCOT study only because I provided it to them.

30. In order to develop new ways to treat the serious conditions facing patients, clinicians need to be able to draw from the resources of the medical community without fear that their discoveries will lose intellectual property protection simply because they included those who provided resources as co-authors on an article describing their work. The Bouabdallaoui reference—a reference on which I am a co-author—is a publication of my invention or substantively the same subject matter of my invention by me with others who obtained the subject matter disclosed therein directly or indirectly from me.

I declare under penalty of perjury under the laws of the United States of America that the foregoing is true and correct. Executed this 16<sup>th</sup> day of October 2023.

  
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Jean-Claude Tardif, M.D.