CADTH REIMBURSEMENT REVIEW

Patient and Clinician Group Input

SOTORASIB (Lumakras)

(Amgen Canada Inc.)

Indication: For the treatment of adult patients with Kirsten rat sarcoma viral oncogene homolog (KRAS) G12C-mutated locally advanced (not amenable to curative therapy) or metastatic non-small cell lung cancer (NSCLC) who have received at least one prior systemic therapy..

September 12, 2022

This document compiles the input submitted by patient groups and clinician groups for the file under review. The information is used by CADTH in all phases of the review, including the appraisal of evidence and interpretation of the results. The input submitted for each review is also included in the briefing materials that are sent to expert committee members prior to committee meetings.

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Patient Input

CADTH Reimbursement Review
Patient Input Template

Name of the Drug and Indication	Sotorasib for the treatment of adult patients with Kirsten rat sarcoma viral oncogene homolog (KRAS) G12C-mutated locally advanced (not amenable to curative therapy) or metastatic non-small cell lung cancer (NSCLC) who have received at least one prior systemic therapy.
Name of the Patient Group	Joint submission by The Lung Health Foundation, Lung Cancer Canada and Canadian Cancer Survivor Network
Author of the Submission	Onai Muvezwa - Lung Health Foundation Winky Yau - Lung Cancer Canada Lindsay Timm - Canadian Cancer Survivor Network

1. About Your Patient Group

This is a joint submission by The Lung Health Foundation, Lung Cancer Canada and the Canadian Cancer Survivor Network.

The Lung Health Foundation (previously named the Ontario Lung Association) is registered with the CADTH and pCODR (www.lunghealth.ca). The Lung Health Foundation (Ontario Lung Association) is a registered charity that assists and empowers people living with or caring for others with lung disease. It is a recognized leader, voice and primary resource in the prevention and control of respiratory illness, tobacco cessation and prevention, and its effects on lung health. The Foundation provides programs and services to patients and health-care providers, invests in lung research and advocates for improved policies in lung health. It is run by a board of directors and has approximately 46 employees, supported by thousands of dedicated volunteers.

Lung Cancer Canada (https://www.lungcancercanada.ca/) is a registered national charitable organization that serves as Canada's leading resource for lung cancer education, patient support, research and advocacy. Lung Cancer Canada is a member of the Global Lung Cancer Coalition and is the only organization in Canada focused exclusively on lung cancer. Lung Cancer Canada is registered with CADTH.

The Canadian Cancer Survivor Network (CCSN) is a national network of patients, families, survivors, friends, community partners, funders, and sponsors who have come together to take action to promote the very best standard of care, whether it be early diagnosis, timely treatment and follow-up care, support for cancer patients, or issues related to survivorship or quality of end-of-life care. https://survivornet.ca/

2. Information Gathering

The Lung Health Foundation, Lung Cancer Canada and the Canadian Cancer Survivor Network collaborated in gathering data included in this submission. Interviews were conducted with patients and caregivers and a survey was created by CCSN to collect quantitative data from people with experience with lung cancer and sotorasib. The survey was open from August 25, 2022, to

September 8, 2022, to obtain responses. All respondents to the survey live in Canada. All of the respondents to the survey identify as female. One of the respondents is a lung cancer patient who has not taken sotorasib and another is a caregiver.

Interviews were conducted by Lung Cancer Canada and The Lung Health Foundation. Of those interviewed, 3 patients had experience with sotorasib, 1 patient with KRAS G12C lung cancer, though she has not taken sotorasib, and a caregiver to a patient with lung cancer who has no experience with sotorasib. All interviews were conducted via phone call, 3 patients and a caregiver are Canadian and one patient is from the United States. Details of each patient and caregiver are listed in the chart below:

Name	Patient/Caregiver	Gender	Diagnosis	Duration on sotorasib	Location
LS	Patient	Female	Stage 4 adenocarcinoma	16 months (May 2021-present)	United States (FL)
MC	Patient	Female	Stage 2B NSCLC (now 4A)	20 months (January 2020 – September 2021)	Nova Scotia
WF	Patient	Female	Stage 4 NSCLC	20 months (January 2021 - present)	British Columbia
RM	Patient	Female	Stage 4 NSCLC	N/A (has not taken sotorasib)	Quebec
GM	Caregiver	Female	Stage 4 NSCLC	N/A	Ontario

3. Disease Experience

In summer 2017, LS had a small cough but didn't think much of it and attributed it to seasonal allergies. A few months later when she hurt her back while moving furniture, she got an x-ray which revealed not only a strained back, but also a shadow in her lung. As more tests were done and her cough got worse, it became clear that it wasn't just pneumonia as the physician initially thought. Although LS continued to work full-time throughout, it became clear that this wasn't looking good. She was officially diagnosed with stage 3B non-small cell adenocarcinoma in March 2018, and started treatment with chemotherapy and radiation, as expanded on in section 4. However, her diagnosis did not stop her career and she continued to work 60+ hours a week during treatment and traveled across the country twice a month. LS progressed 2.5 years after her initial diagnosis, and prior to starting treatment with sotorasib in May 2021, LS felt like she had hit "rock bottom" in her journey. She was on oxygen, had a debilitating cough, could barely eat or talk without needing to catch her breath, and couldn't shower without assistance. She decided to move back to her home state of Florida from Texas and completely relied on friends and family to pack her furniture for the move. She started sotorasib and her life had completely changed, as explained in section 6.

Before RM was diagnosed with stage 4 non-small cell lung cancer in March 2020, she had always been a very active individual and ran her own business with her husband, retiring only a few months before her diagnosis. Treatment with multiple courses of immunotherapy and chemotherapy yielded many mental and emotional side effects on her that have been very difficult for her to cope with, including depression, anxiety, panic attacks, and severe mood swings, which she is still battling to this day, even though she has been in remission with no evidence of disease since June 2022. When asked how she had been feeling throughout her cancer journey, RM responded that she "does not feel like herself, and her mood can take a complete turn in a second. I do not feel like the same RM that I was before, and it's been very difficult on my husband". Although she is currently NED as of September 2022, she knows her cancer could return at any moment and it has been hard for her as a patient to grasp that things may never be the same.

A survey respondent, who is a caregiver, detailed the experience of their loved one. The patient had been diagnosed over two years ago and is currently early stage (1). The patient was diagnosed using CT, MRI, PET, biopsy, and bone scan. In regards to the cancer journey the caregiver had this to say about their experience, "Cancer patients are waiting for lung surgeries all across Canada. They shouldn't have to wait for these very important surgeries. Patients are waiting 6-8 weeks. In that time a lung tumour could grow another centimeter. This is unacceptable, especially when we are trying to find lung cancer in the early stages." We asked the caregiver about the issues that they have encountered as a caregiver for someone with lung cancer, they responded with having experienced fatigue, emotional drain, anxiety/worrying, hours spent in medical appointments, monetary concerns (absence at work, driving expenses, etc.), inability to plan ahead, anger, feeling isolated (difficulty connecting with friends, geographical remoteness), feelings of "doom" due to challenging prognosis, and feelings of helplessness. When asked about how caring for someone has affected their daily routine or lifestyle, the caregiver responded, "My daily lifestyle has been one of worry and anxiety." We asked what the most challenging adverse effect is related to their loved one and their current treatment or therapy, the caregiver said that the surgical wait times was the most difficult part. When asked to share anything else about their experience as a caregiver, they had this piece of advice to share, "To all caregivers make sure you get the support needed either through an online support group or an actual support group. These groups really help to get your frustrations out and you can learn how to better deal with the anxiety and anger."

G.M, a caregiver to a spouse living with lung cancer, reported that she has a challenging time supporting her spouse through lung cancer. Her spouse had some comorbidities, and a lung cancer diagnosis impacted his health significantly. As a caregiver, her responsibilities have included preparing his favourite meals to encourage him to eat well and maintain a healthy weight, making arrangements for special transportation to attend medical appointments and managing the family's day to day responsibilities. She has found the experience of being the primary caregiver challenging mentally, physically and financially. She reported that she feels burnt out and does not have a lot of sources of support.

4. Experiences With Currently Available Treatments

The standard of care for KRAS G12C patients may typically include chemotherapy, radiation, or immunotherapy. WF, LS and MC all had first-line treatment with chemotherapy for roughly 6 months to a year. Although none of the three patients had any major side effects from the treatment, it did not work for all three of them as their disease did not respond to the treatment. After MC had a lobectomy after being diagnosed in March 2019, her initial cough was gone, but by the time she finished first-line treatment with combination pembrolizumab and chemotherapy in October 2019, she developed pneumonitis, felt very sick, and her cough not only returned, but came back even worse than before.

WF had chemotherapy for about a year but her cancer had continued to grow with no response to the treatment. She was then put on immunotherapy for 6-8 months, which similarly did not work, and she thought she was at the end of the line with no options left. She then started on sotorasib via a clinical trial, and continues to be on it today.

One of the survey respondents, a caregiver, stated that the patient was able to utilize surgical therapy as their treatment. When asked about the symptoms or problems that affect the patient's quality of life the caregiver said that fatigue, shortness of breath, and hoarseness or changing voice were all experienced by the patient. When asked about the adverse effects of the current treatment that the patient is receiving, the caregiver responded that the patient had a lobectomy. When asked if they had any difficulties accessing any therapies, the caregiver said that they had not had any issues in accessing therapy. The caregiver was asked if they felt that any of the patient's needs were not yet being met with current therapy and she felt that all needs were met.

Another survey respondent detailed that they are currently receiving treatment through radiation, targeted therapy, and surgical therapy. When asked about the symptoms or problems that affect their quality of life the patient said that they experience pain in chest, shoulder, back, or arms, loss of quality of life, and bone pain or fractures. When asked about the adverse effects of the current treatment that they are receiving, the patient detailed that they have pain and swelling, mouth sores, fatigue, and diarrhea. When asked if they had any difficulties accessing any therapies, the patient stated that they had not had any issues accessing therapy. The patient was asked if they felt that any of their needs were not yet being met with current therapy and they felt that all needs were being met.

G.M reported that her husband received chemotherapy as first line treatment. He had many pre-existing conditions and responded poorly to the chemotherapy, as a result. G.M reports that he experienced weight loss, fatigue, mood changes and declined performance status. Due to the side effects, he had to discontinue treatment and is currently receiving comfort measures only.

5. Improved Outcomes

G.M reported that she is most interested in treatments that help cure cancer while maintaining good quality of life. As a caregiver, she found it very difficult to watch her spouse struggle with the treatment and side effects. She also expressed the importance of treatments that are accessible from home to limit the need for frequent trips to the infusion clinics.

When asked what they hoped a new treatment would address to manage the patient's disease, a survey respondent stated that they hoped a new treatment would maintain quality of life, delay onset of symptoms, give access to a new option for treatment, ease of use, prolong life, improve functionality/mobility, and ultimately provide a cure.

Respondents from the survey hope that a new treatment would allow them to maintain a good quality of life, delay onset of symptoms, give access to a new option for treatment, reduce side effects from current medications or treatments, prolong life, improve functionality/mobility, and ultimately provide a cure.

6. Experience With Drug Under Review

Sotorasib is effective at treating the cancer and maintaining stable disease.

When MC was first diagnosed with stage 2B adenocarcinoma in December 2018, her tumour was fortunately only confined to one lung and did not have any metastases elsewhere. She had a lobectomy done and 2 months later when she was about to start chemotherapy, she had another CT scan done, which unfortunately showed her cancer had quickly spread to her other lung, progressing her to stage 4A disease instead. After finishing her course of chemotherapy, she started treatment with sotorasib in January 2020. Within a week, she already felt much better and in 6 weeks, her first CT scans showed a 65% reduction in her lung tumour, and another small reduction the following 6 weeks. MC attributed sotorasib to be a miracle for her and remained on the treatment for over 1.5 years until September 2021 when her disease progressed and was taken off the trial.
LS was diagnosed March 2018 with metastatic non-small cell lung cancer (adenocarcinoma) and was deemed inoperable as she had also metastasis in her lymph nodes. Prior to starting sotorasib, she had been stable for 23 months while on immunotherapy, but progressed in September 2020 when her upper right lobe had collapsed. LS was told that at this time, her options were limited and there wasn't much to do other than wait for a clinical trial. In May 2021, she started the sotorasib trial and her first scan in 5.5 weeks showed significant reduction in tumour size. Her 2nd scan showed continued reduction and by the 3rd scan, she had a complete response and had no evidence of disease. She continues to be on the treatment in September 2022 and is still currently NED.

WF had surgery to remove her lower right lobe after being diagnosed in 2019, and after previous immunotherapy and chemotherapy treatments did not work, she started on sotorasib in January 2021. Her most recent scans in Summer 2022 show that her cancer had shrunk by 50% and still continues to be on the treatment in September 2022.

Sotorasib is a durable form of treatment.
As mentioned previously, all three patients, WF, LS, and MC were on treatment with sotorasib for over a year, with LS and WF both still on treatment at the time of writing. MC was on sotorasib for 15 months until she developed progression and pneumonia and had to be taken off, but is still doing very well on a different treatment. She mentioned she had never seen such dramatic improvement in her disease with her other treatments as she saw with sotorasib. The reality of these patients show just how incredible sotorasib has been for them, with more real-world evidence certainly out there.

Patients experienced few manageable side effects in comparison to previous treatments.
Patients who had experience with sotorasib noted that the side effects were much more manageable in comparison to other treatments, with 2 noting nearly no side effects at all. LS states the only side effects she's experienced are fatigue, aches and pains when walking for extended periods of time, but all of these are manageable. WF said she had only a small rash that lasted about a week and minor fatigue, but otherwise she felt well.

MC noted all the side effects she experienced were temporary and went away after a month or two, including a minor rash, diarrhea, shortness of breath, and increased liver enzymes. None of the side effects had significant impacts on her life. These side effects all pale in comparison to the harsher systemic treatments like chemotherapy and immunotherapy that carry many more effects.

Patients were able to improve or maintain their quality of life while on sotorasib.
Although fatigue is a common symptom that most patients interviewed reported having, many noted that they have been able to continue living a great quality of life even while on sotorasib, which was not the case while on other treatments like chemotherapy. WF was extremely active and constantly on-the-go before being diagnosed, and although now she gets tired more easily and needs to take frequent breaks, she says her day-to-day life now is very comparable to before diagnosis, and sotorasib has been her lifesaver. Her quality of life has not been impacted at all, she is very independent and continues to run errands daily while on treatment.

Before starting sotorasib, LS was on oxygen, could barely eat or shower without assistance, and overall had a very poor quality of life. Once she started treatment, her symptoms cleared up in about 2 weeks and her quality of life skyrocketed. She has been NED for over a year and recently moved back to her hometown in Florida from Texas to be closer to her family. She has started travelling again, returned to working part-time for her own business, and is also a caregiver for her father. She has been very independent, driving herself to run errands and medical appointments, and overall enjoying a great quality of life. Patients such as LS and WF show that living with a lung cancer diagnosis isn't always negative, and finding success with treatments like sotorasib have given them a second chance at life.

MC is a very outgoing and optimistic individual, and when speaking to Lung Cancer Canada, she repeatedly mentioned that because of the miracle that sotorasib was in treating her disease, she had been maintaining her quality of life and never had too many major setbacks throughout her cancer journey. While taking sotorasib, it was like she wasn't sick at all and no one could really tell the difference had they not known she was a cancer patient. Prior to the pandemic while she was on the treatment, she had to travel to Toronto from her home in Nova Scotia every 3 weeks for medical appointments, and the constant travel was never a problem for her.

She continued to enjoy her life as normal during treatment, and even continued with the clinical trial remotely from home when travel restrictions were in place. MC continues to travel to Toronto frequently to visit her grandchildren, and is even about to permanently move to the city with her husband to be closer to her family. Sotorasib has given patients like LS, MC and WF the opportunity to do activities outside of just being a cancer patient, allowing them to maintain or improve their quality of life and return to the hobbies they love and do things that matter most to them.

The success patients had with sotorasib reassured them a sense of hope and allowed them to make goals and plan for their future.
Although LS is currently NED, she knows that her cancer will eventually come back, and being on sotorasib gives her time for new treatments to be developed, approved, and available for patients like her. She says that she's "living her best life now" and spending much more time with friends, which she hasn't been able to do lately because of the uncertainty of previous treatments.

When WF was diagnosed, she mentioned she felt like she "faced a death sentence" when her doctor gave her a prognosis of only a year, given she had metastatic lung cancer. However, this turned out to be her second cancer diagnosis in her lifetime - she was diagnosed with metastatic breast cancer exactly 11 years before her lung cancer diagnosis, to the exact day. Having an excellent support system with her two adult sons, in-laws, granddaughters, and close friends made things easier for her as she lives alone and allowed her to focus on things that mattered most to her. After previous treatments didn't work, her oncologist thought they had ran out of options until she found success with sotorasib. WF made a promise to herself to continue taking it day-by-day and remain optimistic and filled with hope.

Speaking to Lung Cancer Canada, WF says, "I've had an excellent life. I have no complaints and am doing relatively well given my circumstances. I don't know what comes next but I hope I can continue to be here for my grandchildren, maybe travel again, and just spend time with my loved ones. I'm just happy to take it day-by-day and see what life has to offer".

7. Companion Diagnostic Test

Sotorasib is targeted therapy for patients with the KRAS G12C mutation. This mutation is identified through biomarker testing across Canada.

8. Anything Else?

The approval of sotorasib for KRAS G12C patients in Canada is a huge step forward in the treatment paradigm for advanced non-small cell lung cancer. First-line treatment with immune-checkpoint inhibitors are being incorporated into standard of care more frequently, but once patients progress on these treatments, there are limited second-line options available to them. Sotorasib, as discussed throughout this submission with real-world patient experiences, has induced rapid and durable responses and allowed patients to enjoy a quality of life that is worthwhile and fulfilling while decreasing the caregiver burden. We hope that CADTH takes these patient values and experiences into thoughtful consideration and provides a positive review so patients can move forward and have treatment options like sotorasib that are available when needed.

Appendix: Patient Group Conflict of Interest Declaration

Lung Health Foundation
To maintain the objectivity and credibility of the CADTH reimbursement review process, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest. This Patient Group Conflict of Interest Declaration is required for participation. Declarations made do not negate or preclude the use of the patient group input. CADTH may contact your group with further questions, as needed.

1. Did you receive help from outside your patient group to complete this submission? If yes, please detail the help and who provided it.

No

2. Did you receive help from outside your patient group to collect or analyze data used in this submission? If yes, please detail the help and who provided it

No

3. **List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review**.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
N/A				

I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this patient group with a company, organization, or entity that may place this patient group in a real, potential, or perceived conflict of interest situation.

Name: Peter Glazier

Position: Executive Vice President

Patient Group: Lung Health Foundation/Ontario Lung Association

Date: September 9,2022

Appendix: Patient Group Conflict of Interest Declaration

Lung Cancer Canada
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6. **List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review**.

Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Amgen				X

I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this patient group with a company, organization, or entity that may place this patient group in a real, potential, or perceived conflict of interest situation.

Name: Shem Singh

Position: Executive Director

Patient Group: Lung Cancer Canada

Date: September 9, 2022

Appendix: Patient Group Conflict of Interest Declaration

Canadian Cancer Survivor Network

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No

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Company	Check Appropriate Dollar Range			
	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Amgen 2021			x	
Amgen 2022			x	

I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this patient group with a company, organization, or entity that may place this patient group in a real, potential, or perceived conflict of interest situation.

Name: Lindsay Timm

Position: Communications and Administration Coordinator

Patient Group: Canadian Cancer Survivor Network

Date: September 9, 2022

Clinician Input

Clinician Group Input #1

CADTH Project Number: PC0300-000

Generic Drug Name (Brand Name): sotorasib (Lumakras)

Indication: Treatment of adult patients with Kirsten rat sarcoma viral oncogene homolog (KRAS) G12C-mutated locally advanced (not amenable to curative therapy) or metastatic non-small cell lung cancer (NSCLC) who have received at least one prior systemic therapy.

Name of Clinician Group: Lung Cancer Drug Advisory Committee

Author of Submission: Dr. Pete Ellis

1. About Your Clinician Group

OH-CCO's Drug Advisory Committees provide timely evidence-based clinical and health system guidance on drug-related issues in support of CCO's mandate, including the Provincial Drug Reimbursement Programs (PDRP) and the Systemic Treatment Program.

2. Information Gathering

The information was jointly discussed via email.

3. Current Treatments and Treatment Goals

Currently, patients with K-ras G12C mutated advanced lung cancer may be treated with various drug and non-drug treatments, including palliative radiation therapy, palliative care, and systemic therapy. Systemic therapies include immunotherapy and platinum based doublet chemotherapy, either in sequence if PD-L1 is over 50% on tumour, or concurrently. After progression on doublet chemotherapy and immunotherapy, taxane based therapy such as docetaxel is considered a standard treatment.

Although there are "ideal treatments" based on clinical trials, the majority of patients with advanced lung cancer historically, and a large proportion of these patients today, do not receive any systemic anti-cancer therapy. Current treatments, including platinum chemotherapy, taxane therapy, and immune therapy, are either contra-indicated or considered not acceptable in a large portion of cancer patients. Even for patients who receive platinum doublet therapy, less than 1/2 are subsequently treated with docetaxel

therapy, despite an approximately 4 month improvement in median overall survival in the pivotal trials. This speaks to the desire of many patients to avoid intravenous drugs with potentially toxic side effects.

Platinum-based chemotherapy and immune checkpoint inhibitors represent the most commonly used systemic therapies in patients with metastatic NSCLC. Following progression on these agents, some patients may receive further chemotherapy with docetaxel. However, many patients may not receive further systemic therapy. Supportive care is done as patients cancer progresses and the patient dies. Patients with lung cancer may die in various ways, but often with a period before death of increasing care needs, inability to work and care for themselves and families, and hospitalizations.

Current treatments such as immunotherapy and chemotherapy are meant to improve symptoms and prolong life. When best supportive care and no further systemic therapy is available, treatments are meant to target symptoms and not underlying disease mechanism.

A treatment such as sotorasib in this setting would be used in patients who have received prior platinum-based chemotherapy and an immune checkpoint inhibitor (and possibly docetaxel), unless there are contraindications to these agents. Goals of therapy would be to reduce tumour burden, and improve symptoms and potentially prolong life-acknowledging their values and desires.

4. Treatment Gaps (unmet needs)

4.1. Considering the treatment goals in Section 3, please describe goals (needs) that are not being met by currently available treatments.

The currently available treatments prolong life and delay disease progression in most patients who receive them, but not all patients respond, virtually all patients eventually progress, and no treatments in the chemotherapy and immunotherapy refractory setting are available to meaningfully prolong life. Currently available treatments such as intravenous immunotherapy, and chemotherapy with doublet chemotherapy and taxane monotherapy as second/third line are not feasible or tolerated in many patients, and an oral anti-cancer treatment that slows disease process is needed to ideally improve length of life and quality of life. An oral option without chemotherapy and it's side effects and life-impact is needed, as currently available treatments still not used/considered acceptable in a large number of patients.

5. Place in Therapy

5.1. How would the drug under review fit into the current treatment paradigm?

This would be an entirely new line of therapy. It would not be used simultaneously with chemotherapy or immunotherapy. It would be used in patients who have progressed or intolerant of platinum-based chemotherapy and immunotherapy (where appropriate) and possibly docetaxel.

There would not be a meaningful impact on immunotherapy or doublet platinum chemotherapy use, there may be a slight decrease in taxane use in this population. The drug may be preferentially moved prior to docetaxel therapy if the CODEBREAK200 trial, which is expected shortly, indicates a meaningful improvement in survival or quality of life. As mentioned earlier, docetaxel in clinical trials did show a meaningful improvement in OS compared to best supportive care and to other chemotherapy regimens (ifosfamide), but is not used due to anticipated side effects in many patients.

It would be appropriate for clinicians to discuss with patients immunotherapy, doublet chemotherapy, and docetaxel chemotherapy, as therapies with a known survival advantage and quality of life advantage over best supportive care. It would be appropriate to recommend that clinicians should discuss and offer these options to patients, but it is not appropriate to say patients MUST try these treatments, as this is coercive and not patient centered care. Clearly, standard of care therapies are not considered acceptable by a large proportion of patients, as documented by real world utilization data.

5.2. Which patients would be best suited for treatment with the drug under review? Which patients would be least suitable for treatment with the drug under review?

Patients with non-squamous Kras G12C mutation, advanced, with no other appropriate systemic lines of therapy. Patients with squamous cell with light smoking/non-smoking will likely also be tested as is standard. (Is this getting too complicatd. Is it simpler to say that sotorasib would be a treatment option in any patient with advanced NSCLC with a tumor known to have a KRAS G12C mutation, who has received prior therapy. Stage IV/recurrent. Patients would be identified from typically tissue or blood based testing documenting a G12C mutation. The companion diagnostics are typically done by NGS in Ontario. Misdiagnosis does not occur. It is only possible to identify those with a Kras G12C mutation.

5.3 What outcomes are used to determine whether a patient is responding to treatment in clinical practice? How often should treatment response be assessed?

Typically yes, but clinical trials use RECIST critieria that are meant for clinical trials, not clinical practice. In clinical practice a combination of clinical judgement, radiological interpretation, and clinically standardized scales such as ESAS etc. are used to determine if a patient is benefitting from their therapy. RECIST (and it's derivatives) were never devised to determine if patient should continue or discontinue treatment, but to access activity of drugs in phase II trials.

A clinically meaningful response would be improvement in symptoms, stable disease, or tumour shrinking on CT scan, and prolonged survival. In terms of what is a clinically meaningful improvement in frequency or severity of symptoms, this will vary amongst patients somewhat, and some variation across physicians.

5.4 What factors should be considered when deciding to discontinue treatment with the drug under review?

Loss of clinical benefit such as unequivocal disease progression (symptoms, poly-progression etc.) or intolerable side effects

5.5 What settings are appropriate for treatment with [drug under review]? Is a specialist required to diagnose, treat, and monitor patients who might receive [drug under review]?

Outpatient clinic. Some cases of in hospital administration if in hospital for a non-cancer reason. Sotorasib should be supervised by a medical oncologist, or respirologist involved in the treatment and supervision of patients with lung cancers

6. Additional Information

N/A

7. Conflict of Interest Declarations

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Did you receive help from outside your clinician group to complete this submission? If yes, please detail the help and who provided it.

Yes. Ontario Health provided secretariat functions to the DAC.

Did you receive help from outside your clinician group to collect or analyze any information used in this submission? If yes, please detail the help and who provided it.

No.

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review. **Please note that this is required for each clinician who contributed to the input — please add more tables as needed (copy and paste). It is preferred for all declarations to be included in a single document.**

Declaration for Clinician 1

Name: Dr. Peter Ellis

Position: Member, Lung Cancer Drug Advisory Committee

Date: 29/08/2022

☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 1: Conflict of Interest Declaration for Clinician 1

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
NA				

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 2

Name: Dr. Stacey Hubay

Position: Member, Lung Cancer Drug Advisory Committee

Date: 29/08/2022

☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 3: Conflict of Interest Declaration for Clinician 3

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
NA				

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 3

Name: Dr. Andrew Robinson

Position: Member, Lung Cancer Drug Advisory Committee

Date: 29/08/2022

☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 4: Conflict of Interest Declaration for Clinician 4

	Check appropriate dollar range*			
Company	**$0 to $5,000**	**$5,001 to $10,000**	**$10,001 to $50,000**	**In excess of $50,000**
NA				

* Place an X in the appropriate dollar range cells for each company.

Clinician Group Input #2

CADTH Project Number: PC0300-000
Generic Drug Name (Brand Name): sotorasib (Lumakras)
Indication: Treatment of adult patients with Kirsten rat sarcoma viral oncogene homolog (KRAS) G12C-mutated locally advanced (not amenable to curative therapy) or metastatic non-small cell lung cancer (NSCLC) who have received at least one prior systemic therapy.
Name of Clinician Group: Lung Cancer Canada – Clinician Group
Author of Submission: Dr. Rosalyn Juergens (lead), Dr. Geoffery Liu, Dr. Quincy Chu, Dr. Mahmoud Abdelsalam, Dr. Kevin Jao, Dr. Dorothy Lo, Dr. Ron Burkes, Dr. Lacey Pitre, Dr. Randeep Sangha, Dr. David Stewart, Dr. David Dawe, Dr. Brandon Sheffield, Dr. Normand Blais, Dr. Nathalie Daaboul, Dr. Sunil Yadav, Dr. Barb Melosky, Dr. Catherine Labbé, Dr. Stephanie Snow, Dr. Paul Wheatley-Price, Dr. Jefferey Rothenstein, Dr. Mark Vincent, Dr. Parneet Cheema, Dr. Shaqil Kassam, Dr. Jawaid Younus, Dr. Diana Ionescu, Dr. Silvana Spadafora

1. About Your Clinician Group

Lung Cancer Canada (LCC) is a national charity with the purpose of increasing awareness about lung cancer, providing support and education to lung cancer patients and their families, to support research and to advocate for access to the best care for all lung cancer patients in all provinces and territories. Through the LCC Medical Advisory Committee (MAC), we have been providing clinician input for submissions of new lung cancer drugs to the HTA process for many years. The LCC MAC is made up of clinicians and key opinion leaders in the field of lung cancer across the country. www.lungcancercanada.ca

2. Information Gathering

The information gathered to support this submission was collected through a review of the literature available in PubMed as well as meeting proceedings from recent AACR, ASCO, ESMO and WCLC conferences.

3. Current Treatments and Treatment Goals

The current standard of care for treatment-naïve advanced or metastatic non-small cell lung cancer (mNSCLC) based on reimbursement in the majority of the provinces for patients whose tumours harbour K-ras G12C mutations includes:
1. platinum doublet chemotherapy based on histology;
2. platinum doublet chemotherapy plus pembrolizumab for those with PDL-1 expression <50%, and possibly those with PDL-1 expression $\geq$ 50% who are non-smokers, female, high disease or symptom burden; and
3. pembrolizumab alone for those with PDL-1 expression $\geq$ 50%.

Options 2 and 3 are contraindicated in those who have active autoimmune disease or who have organ or bone marrow transplantation on active immunosuppressants.

<u>For mNSCLC patients who progressed on prior systemic therapy, the options include:</u>
1. Platinum doublet for those who had received pembrolizumab as first-line therapy,
2. Anti-PD(L)1 therapy, including pembrolizumab, nivolumab and atezolizumab, for those who had received platinum/pemetrexed as first-line therapy (but with the adoption of platinum doublet and pembrolizumab as first-line therapy, this represents a very small number of patients), and
3. Docetaxel for those who have progressed on platinum doublet and anti-PD(L)1 therapy. Docetaxel comprises the vast majority of treatment in the 2nd line setting in Canada.

Chemotherapy is palliative in the metastatic setting and can improve symptoms but is not curative in intent. Immunotherapy has the opportunity for dramatic improvements in overall survival achieved mainly in patients who are highly PD-L1 positive. We, at this time, do not consider this treatment curative but it is clearly disease modifying. Immunotherapy has shifted to the front line setting for the majority of patients either as a single agent or in combination with platinum doublet chemotherapy. The mainstay of treatment in the second line setting is comprised of single agent chemotherapy with docetaxel. Docetaxel is not disease modifying.

In the advanced or metastatic NSCLC setting, the goals of therapy are, in the order of priority,
1. Improvement in mOS: the most conclusive endpoint for all anti-cancer systemic therapy.
2. Rapidity of and prolonged improvement in lung cancer related symptoms measured by median time-to-response, ORR, or progressive disease rate and mPFS: As the majority of advanced or metastatic NSCLC are symptomatic at the time of initial diagnosis and at the time of progression from prior therapy, early and prolonged symptoms improvement without disease progression radiologically will provide clinically relevant improvement in health-related quality-of-life.
3. Toxicity: Incidences of Grade 2 toxicity experienced daily and Grade 3 or higher clinically important toxicity and dose reduction or dose discontinuation are especially important to consider for any systemic therapy. Metastatic NSCLC patients have high symptom burden, treatment can further impair patient well-being in the setting of frequent and clinically significant toxicity.
4. Resource utilization: Intravenous systemic therapy is given every 3-6 weeks, requiring resources for clinical assessment, laboratory investigation and drug administration for 1-3 hours, depending on the regimen used. But oral therapy can potentially

reduce resources used, especially if there is a low incidence of grade 2 toxicity requiring clinical intervention and grade 3 or 4 toxicity. This is especially important in the Canadian setting due to clinic and chemotherapy administration space constraints.

4. Treatment Gaps (unmet needs)

4.1. Considering the treatment goals in Section 3, please describe goals (needs) that are not being met by currently available treatments.

The agent being evaluated in this application, sotorasib, is requesting an indication in the second line setting so the most appropriate comparator is docetaxel in the Canadian context.

1. Improvement in mOS: Docetaxel has been shown to improve overall survival through a randomized phase III clinical trial in comparison to best supportive care (TAX317: Shepherd *JCO* 2000). In the TAX317 trial there was an overall survival benefit of 2.4 months [7 months (docetaxel) vs 4.6 months (best supportive care)]. In a more contemporary study of patients with stage IV lung cancer of non-squamous histology (K-ras G12C is found mainly in patients with adenocarcinomas) the median overall survival of patients randomized to docetaxel is 9.4 months (Borghaei *NEJM* 2015). This modest benefit in overall survival is often not compelling for patients when they weigh this benefit against the risk of toxicity discussed below.
2. Rapidity of and prolonged improvement in lung cancer related symptoms measured by median time-to-response, ORR, or progressive disease rate and mPFS: The response rate for docetaxel is low and has ranged between 7-12% from the registrational trial as well as in trials where docetaxel serves as the modern control group (TAX317: Shepherd *JCO* 2000; Checkmate57: Borghaei *NEJM* 2015). The durability of responses when achieved ranges between 5 and 6 months on average. Median progression free survival was measured at 10.6 weeks in the in TAX317 trial and 18 weeks in the Checkmate57 trial. Progressive disease is the best response in 29-34% of patients in these studies.
3. Toxicity: Side effects of docetaxel are well established. Toxicities in modern studies include: neutropenia (in 31% of patients), fatigue (in 29%), nausea (in 26%), alopecia (in 25%) and diarrhea (in 23%). Patients also experience neuropathy, edema, anorexia and asthenia. Grade 3 or 4 toxicities are reported in 18% of patients in the example of the Checkmate57 trial. Treatment related death from febrile neutropenia related to docetaxel was reported in both the TAX317 and Checkmate57 trials – 1 patient in each trial (rate < 1%).
4. Resource utilization: Docetaxel is an intravenous treatment given once every 3 weeks. The mean number of cycles of treatment is 4 in clinical trials. Docetaxel infusions carry a risk of allergic reaction so standard Canadian practice is to titrate up the rate over the initial 2-3 cycles of treatment with infusion times taking on average 2 hours. The risk of febrile neutropenia is approximately 10% which would generally lead to hospitalization and further resource utilization. Patients are generally expected to come in for toxicity assessment including blood work with each cycle of treatment and generally chemotherapy is given on an alternate day 1-2 days subsequently.

To summarize the gaps, while there is an overall survival benefit over best supportive care, the survival improvement is marginal. Only the minority of patients respond to treatment and three times as many patients have primary progressive disease. Toxicity risk is high requiring frequent dose modification and treatment discontinuation (26% and 15% in Checkmate57 respectively). The treatment is resource intensive and is not disease modifying.

5. Place in Therapy

5.1. How would the drug under review fit into the current treatment paradigm?

Presence of K-ras mutations in mNSCLC have been known since 1987 (Rodenhuis *NEJM* 1987). Consistently, presence of K-ras mutations has been associated with poorer prognosis. Several studies have recently been published assessing the natural history of patients with K-ras mutations (Spira *Lung Cancer* 2021; Scharpf *Cancer Res* 2022; Sebastian *Lung Cancer* 2021). Patients with K-ras mutant lung cancer most commonly have adenocarcinoma histology, have a history of tobacco use, are more likely to present with metastatic disease including a higher rate of brain metastases compared to patients without K-ras mutated tumours. These patients have a poorer prognosis and access to better treatment options is a huge unmet need especially in the pre-treated setting. The results of the CodeBreaK100 trial lung cancer cohort were updated at the AACR meeting in 2022 by Dr. Grace Dy. The global phase II CodeBreaK100 trial enrolled patients with advanced or metastatic KRAS G12C–mutated NSCLC who were pretreated with at least one prior systemic therapy or who were ineligible/intolerant to prior therapy. Patients enrolled had 1-3 prior lines of treatment. Over 80% of patients had received both platinum doublet and immunotherapy. The pooled analysis included 174 patients enrolled in phase I (n = 48) and II (n = 126) of the study who were treated with sotorasib at 960 mg orally once daily. At the time of that update, the median time to response was 6 weeks. The centrally confirmed objective response rate was 40.7%, and the disease-control rate was 83.7%. The median duration of response was 12.3 months; 50.6% of responders remained in response for 12 months or more. Median progression-free survival was 6.3 months. The updated analysis of CodeBreaK 100 lung cancer cohort showed no change in median overall survival, which remained 12.5 months. The 1-year overall survival was 50.8%, and the 2-year overall survival was 32.5%.

The toxicity profile of sotorasib is similar to many other targeted therapies oncologists are accustomed to managing with other molecular subtypes of mNSCLC. A total of 70% of patients experienced any treatment-related adverse event; grade 3 or 4 treatment-related adverse events occurred in 21%. Treatment related adverse events led to dose modification in 22% of patients

and treatment discontinuation in 7%. No fatal treatment-related adverse events were identified in the lung cancer cohort. One fatal treatment-related adverse events of interstitial lung disease was reported in this trial in another tumour indication.
Treatment-related adverse events occurring in more than 10% of patients included diarrhea (31%), elevated liver enzymes (18%), nausea (16%), and fatigue (12%). Most adverse events were grade 1 or 2. There was no delayed onset of adverse events, contrary to what we would expect with chemotherapy or immunotherapy. Minimal or no cumulative toxicity contrasts with what we would expect with docetaxel.

CodeBreaK 200 is a global phase 3 randomized active-controlled study comparing sotorasib to docetaxel in K-ras G12C-mutated NSCLC, and has completed enrollment of 345 patients. Eligible patients had previously treated, locally advanced and unresectable or metastatic KRAS G12C-mutated NSCLC. The primary endpoint is progression-free survival and key secondary endpoints include overall survival, objective response rate, and patient-reported outcomes. A press release announced on August 30, 2022 that this study has met its primary endpoint of progression-free survival.

This represents the first randomized data of a KRAS G12C inhibitor. The first results of the CodeBreaK 200 trial were formally presented on 12 September 2022 at the European Society of Medical Oncology (ESMO) annual meeting in the Presidential Symposium 3 as Late Breaking Abstract 10. Median age of patients in this global trial was 64 years. At a median study follow-up of 17.7 months, the study met its primary endpoint of a statistically significant improvement in PFS with sotorasib vs docetaxel (HR, 0.66 [95% CI: 0.51, 0.86], P-value, 0.002). One-year PFS was 24.8% for sotorasib vs 10.1% for docetaxel, and PFS benefit was consistent across subgroups, in particular good disease control in patients with CNS disease. Response rate was significantly improved for sotorasib vs docetaxel (28.1% vs 13.2%, respectively; P<0.001), with a disease control rate of 83% for sotorasib vs 60% for docetaxel. Responses were generally rapid (1.4 month time to response) with a median duration of response of 8.6 months.

There is no OS difference reported, but the study was underpowered for this, and 34% of docetaxel patients subsequently received sotorasib.

Importantly the rates of adverse events and serious adverse events, despite a longer duration of treatment, were fewer in those treated with sotorasib compared to docetaxel.

Consequently, this research demonstrates and confirms that sotorasib has superior efficacy and quality of life, and reduced side effects, when compared to docetaxel. It is a practice changing study and should become the second-line standard of care for patients with advanced KRAS G12C NSCLC.

The requested indication is for treatment of adult patients with Kirsten rat sarcoma viral oncogene homolog (K-ras) G12C-mutated locally advanced (not amenable to curative therapy) or metastatic non-small cell lung cancer (NSCLC) who have received at least one prior systemic therapy. Sotorasib is the first in class small molecule that specifically and irreversibly inhibits K-ras G12C. At this time sotorasib has been studied as a single agent mainly in previously treated patients. Combination studies are underway but are outside the scope of this health technology assessment. We concur with the recommendation that sotorasib, given the current data, is appropriate for patients who have received at least one prior line of treatment. Access to sotorasib is a change in the paradigm of management of K-ras G12C mutated mNSCLC providing the first therapy targeted at the mutation molecularly driving this cancer type.

5.2. Which patients would be best suited for treatment with the drug under review? Which patients would be least suitable for treatment with the drug under review?
The only appropriate mNSCLC patients to be treated with sotorasib are those whose tumour (histology or cytology) or circulating tumour DNA in blood have documented K-ras G12C mutation detected by a validated molecular diagnostic test, preferably next generation sequencing (NGS). This companion diagnostic evaluation is mandatory. Single analyte testing would be prohibitively costly especially in light of the number of known driver mutations in lung adenocarcinomas. Ability to determine K-ras mutation status has become accessible across the country over the past year in lung cancer as NGS platforms have increasingly received provincial funding.
Therapy with sotorasib is not applicable to patients whose tumour does not harbor a K-ras G12C mutation. We do recommend repeat NGS testing in those patients with preserved performance status after initial treatment who have had panels that did not test for K-ras mutations to prevent underdiagnosis. Consideration should be given to appropriate ongoing funding for pathology and molecular genetics to support testing across all the mutation driven sub-populations in mNSCLC.

Appropriate identification of the correct K-ras mutation is critical for therapeutic success. K-ras G12C mutations are the most common subtype of K-ras mutation in mNSCLC (12-13% of adenocarcinoma histology) but very similar sounding mutations such as G12D, G12V and G12A are also present. Only those with the G12C variant can potentially benefit. Well annotated synoptic biomarker reporting is crucial to ensure all clinicians can readily interpret molecular testing reports that are completed.
There are currently no other clinical or pathologic features beyond presence of the K-ras G12C mutation that are known to predict which patients are most likely to benefit from sotorasib. It is debatable whether ECOG 3-4 patients would benefit. Docetaxel

chemotherapy is absolutely contraindicated in poor performance status so these patients have no alternative to best supportive care. Typically access to treatment is restricted to those with performance status of at least 2 or better.

5.3 What outcomes are used to determine whether a patient is responding to treatment in clinical practice? How often should treatment response be assessed?
In clinical practice, the definition of a clinically meaningful response to anti-cancer therapy such as sotorasib is defined as:
1. documentation of lung cancer-related symptoms stabilization or improvement by frequency and severity with or without radiological evidence of tumour shrinkage, or
2. documentation of radiographic reduction of documented sites of known disease at baseline.
CT imaging is the standard with response determined by the treating physician. This assessment modality would be similar to investigator assessed treatment response in clinical trials.
Response to other oral tyrosine kinase inhibitors in Canada is typically assessed every 2-3 months. Given the initial response to sotorasib is usually seen by 6 weeks, this standard would be appropriate.

5.4 What factors should be considered when deciding to discontinue treatment with the drug under review?
In clinical practice, sotorasib will continue until one or more of the following conditions is/are fulfilled:
1. Toxicity despite multiple dose reductions
2. Patient wishes
3. Concurrent medical condition(s) that will jeopardize patient safety while receiving sotorasib
4. Disease progression except:
a. those who have oligoprogression that are amendable to local therapy such as radiation or surgery. Based on study by Gomez et al. from MD Anderson Cancer Centre, patients who experienced oligoprogression had an improvement in both mPFS (14.2 months versus 4.4 months. P=0.022) and mOS (37.6 months versus 9.4 months, p=0.034) with aggressive local therapy over observation or continuation of systemic therapy. See Canadian consensus statement on this (Laurie, S. et al. Curr Oncol. 2019 Feb;26(1):e81-e93)
b. those who have newly diagnosed or progression of brain metastases who should continue with sotorasib after receiving brain radiation or surgery if appropriate.
c. those who have asymptomatic disease. Our Canadian (and global practice) for patients with driver mutations is to continue treatment until there is no longer clinical benefit as represented by overt progression on imaging associated with increased symptom burden.

5.5 What settings are appropriate for treatment with sotorasib Is a specialist required to diagnose, treat, and monitor patients who might receive sotorasib?
To appropriately select patients for sotorasib, molecular testing to identify the K-ras G12C mutation needs to be completed. Next generation sequencing that includes K-ras testing is available across the country. Treatment with sotorasib can be managed by any certified medical oncologist or by general practitioners in oncology under medical oncology supervision. As this is an oral outpatient treatment, this enables access to patients in all jurisdictions of Canada. Monitoring can be done with basic laboratory testing, clinician assessments and CT imaging – all of which is generally accessible.

6. Additional Information

Sotorasib is the first in class K-ras G12C direct inhibitor. The CodeBreaK100 trial has shown an excellent response rate that is four times that of the current standard of care in the second line setting. The durability of these responses is clinically meaningful. The toxicity profile is manageable. The treatment provides an oral therapy which aligns with patient values especially in the platinum refractory setting. The results of the phase III trial has reported a positive outcome for progressive-free survival which is the trial's primary endpoint. We strongly support the funding of sotorasib for this indication. These patients have a poor prognosis and better treatment options is a huge unmet need.

7. Conflict of Interest Declarations

To maintain the objectivity and credibility of the CADTH drug review programs, all participants in the drug review processes must disclose any real, potential, or perceived conflicts of interest. This conflict of interest declaration is required for participation. Declarations made do not negate or preclude the use of the clinician group input. CADTH may contact your group with further questions, as needed. Please see the *Procedures for CADTH Drug Reimbursement Reviews* (section 6.3) for further details.

Did you receive help from outside your clinician group to complete this submission? If yes, please detail the help and who provided it.
No

Did you receive help from outside your clinician group to collect or analyze any information used in this submission? If yes, please detail the help and who provided it.
No

List any companies or organizations that have provided your group with financial payment over the past two years AND who may have direct or indirect interest in the drug under review. Please note that this is required for each clinician who contributed to the input — please add more tables as needed (copy and paste). It is preferred for all declarations to be included in a single document.

Declaration for Clinician 1

Name: Dr. Rosalyn Juergens
Position: Chair, LCC Medical Advisory Committee; Medical Oncologist, Juravinski Cancer Center
Date: Sept 12, 2022

☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 5: Conflict of Interest Declaration for Clinician 1

	Check appropriate dollar range*			
Company	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
Bristol Myers Squibb	x			
Astra Zeneca		x		
Merck Sharp and Dohme	x			
Roche	x			

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 2

Name: Brandon Sheffield
Position: Pathologist, William Osler Health System
Date: 27-07-2022

☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 5: Conflict of Interest Declaration for Clinician 2

	Check appropriate dollar range*			
Company	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
Amgen			X	
AstraZeneca			X	
Bayer			X	
Biocartis			X	
Boehringer-Ingelheim			X	
Cell Marque			X	
Elevation Oncology			X	

Eli Lily			X	
EMD Serono			X	
Incyte			X	
Janssen			X	
Merck			X	
Novartis			X	
Pfizer			X	
Roche			X	
Thermo Fisher			X	
Turning Point Therapeutics			X	

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 3

Name: Dorothy Lo
Position: Medical oncologist, St. Joseph's Health Centre Toronto
Date: 30 June, 2022

☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 5: Conflict of Interest Declaration for Clinician 3

	Check appropriate dollar range*			
Company	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
Merck	X			
BMS	x			
Sanofi	x			
Novartis	x			
astellas		x		
Eisai	x			
Astra Zeneca	x			

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 4

Name: Lacey Pitre
Position: Medical Oncologist, Systemic Therapy Lead - Northeast Region, CCO/Ontario Health
Date: <18-04-2022>

☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 5: Conflict of Interest Declaration for Clinician 4

	Check appropriate dollar range*			
Company	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
Novartis Ribbon Program 2018	X			
MERCK Oncology Speaker's honoraria 2017	X			
EMD Serono Speaker's honoraria 2018	X			
MERCK Oncology Speaker's honoraria 2021	X			
Astra Zeneca Speaker's honoraria 2021	X			

Astra Zeneca Speaker's honoraria 2022	X			
Fuse Health Advisory Board 2017	X			
Novartis Advisory Board 2018	X			
Astella's Oncology Advisory Board 2016	X			

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 5

Name: Dr. Stephanie Snow
Position: President, Lung Cancer Canada; Medical Oncologist, The QEII Health Sciences Center
Date: Sept 12, 2022
☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 5: Conflict of Interest Declaration for Clinician 5

	Nature or description of activities or interests	Check Appropriate Dollar Range			
		$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Amgen	Advisory Role	☒	☐	☐	☐
Astra Zeneca	Advisory Role	☐	☐	☒	☐
Bayer	Advisory Role	☐	☒	☐	☐
Boehringer Ingeiheim	Advisory Role	☒	☐	☐	☐
Bristol-Myers Squibb	Advisory Role	☐	☐	☒	☐
Eisai	Advisory Role	☒	☐	☐	☐
Merck	Advisory Role	☐	☐	☒	☐
Novartis	Advisory Role	☒	☐	☐	☐
Pfizer	Advisory Role	☒	☐	☐	☐
Purdue	Advisory Role	☒	☐	☐	☐
Roche	Advisory Role	☐	☐	☒	☐
Taiho	Advisory Role	☒	☐	☐	☐
Takeda	Advisory Role	☐	☒	☐	☐

Declaration for Clinician 6

Name: Dr. Paul Wheatley-Price
Position: Medical Oncologist, The Ottawa Hospital. Associate Professor, Department of Medicine, University of Ottawa
Date: Sept 12, 2022

☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 5: Conflict of Interest Declaration for Clinician 6

	Check appropriate dollar range*			
Company	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
Sanofi	X			
Astra Zeneca	X			
Jazz Pharmaceuticals	X			
Amgen	X			
Janssen	X			
Novartis	X			
Merck	X			
BMS	X			
Roche	X			
EMD Serono	X			
Pfizer	X			
Bayer	X			
Novartis	X			

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 7

Name: Dr. Geoffrey Liu
Position: Medical Oncologist, Princess Margaret Cancer Centre
Date: Sept 12, 2022

☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 5: Conflict of Interest Declaration for Clinician 7

Company	Nature or description of activities or interests	Check Appropriate Dollar Range			
		$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Takeda Canada	Advisory Board, Health Technology Assessment Submission Advice, Speaker's Bureau, past 10 years	☐	☐	☒	☐
Takeda Canada	(To institution, not individual) Observational Study funding, past 10 years	☐	☐	☐	☒
Hoffman La Roche	Advisory Board, Health Technology Assessment Submission Advice, past 10 years	☐	☐	☒	☐
Pfizer	Advisory Board, Health Technology Assessment Submission Advice, part 10 years	☐	☐	☒	☐
AstraZeneca	Advisory Board, Health Technology Assessment Submission Advice, Speaker's Bureau, past 10 years,	☐	☐	☒	☐
AstraZeneca	(To institution, not individual) Observational Study funding, past 10 years	☐	☐	☐	☒
Bristol Myers Squibb	Advisory Board	☒	☐	☐	☐

Boehringer Ingerheim	(To institution, not individual) Observational Study funding, past 10 years	☐	☐	☒	☐
Abbvie	Advisory Board, past 10 years	☐	☒	☐	☐
Merck	Advisory Board, Health Technology Assessment Submission Advice, past 10 years	☐	☒	☐	☐
EMD Serono	Speaker's Bureau, past 10 years	☒	☐	☐	☐
Novartis	Advisory Board,past 10 years	☐	☐	☒	☐
Glaxo Smith Kline	Advisory Board, past 10 years	☐	☒	☐	☐

Declaration for Clinician 8

Name: Dr Jeffrey Rothenstein
Position: Medical Oncologist, Lakeridge Health
Date: Sept 12, 2022

☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 5: Conflict of Interest Declaration for Clinician 8

	Check appropriate dollar range*			
Company	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
Roche	x			

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 9

Name: Dr Normand Blais
Position: Medical Oncologist, Hôpital Notre Dame du CHUM
Date: Sept 12, 2022

☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 5: Conflict of Interest Declaration for Clinician 9

	Check appropriate dollar range*			
Company	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
Novartis	x			

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 10

Name: Dr. David Dawe
Position: Medical Oncologist, CancerCare Manitoba
Date: Sept 12, 2022

☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 5. Conflict of Interest Declaration for Clinician 10

		Check Appropriate Dollar Range			

Name of Organization	Nature or description of activities or interests	$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
AstraZeneca	Advisory boards	☒	☐	☐	☐
Merck	Advisory Boards	☒	☐	☐	☐
AstraZeneca	Research Grant	☐	☐	☒	☐
Boehringer-Ingelheim	Honoraria	☒	☐	☐	☐

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 11

Name: Dr Randeep Sangha
Position: Medical Oncologist, Cross Cancer Institute
Date: Sept 12, 2022

☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 5: Conflict of Interest Declaration for Clinician 11

	Check appropriate dollar range*			
Company	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
NA				

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 12

Name: Dr Catherine Labbé
Position: Head of Respiratory Medicine Service, Université de Laval
Date: Sept 12, 2022

☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 5: Conflict of Interest Declaration for Clinician 12

	Check appropriate dollar range*			
Company	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
Amgen	X			
Astra Zeneca		X		
Brystol-Myers Squibb Jazz Pharmaceuticals LEO Pharma Merck Pfizer Roche Sanofi Genzyme	X X X X X X X			

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 13

Name: Dr Sunil Yadav
Position: Medical Oncologist, Saskatoon Cancer Centre
Date: Sept 12, 2022

☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 5: Conflict of Interest Declaration for Clinician 13

Bristol-Myers Squibb	Nature or description of activities or interests	Check Appropriate Dollar Range			
		$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	
Bristol-Myers Squibb	Advisory Board	☒	☐	☐	
Astra Zeneca	Advisory Board and Speaking	☒	☐	☐	☐
Merck	Advisory Board and Speaking	☐	☐	☒	☐
Roche	Advisory Board and Speaking	☐	☒	☐	☐
Takeda	Advisory Board and Speaking	☒	☐	☐	☐

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 14

Name: Dr. Quincy Chu
Position: Medical Oncologist, Cross Cancer Institute
Date: Sept 12, 2022

☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 5: Conflict of Interest Declaration for Clinician 14

Bristol-Myers Squibb	Nature or description of activities or interests	Check Appropriate Dollar Range			
		$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Abbvie	Advisory Board and Honoraria	☒	☐	☐	☐
Amgen	Advisory Board and Honoraria	☒	☐	☐	☐
Astra Zeneca	Advisory Board and Honoraria	☐	☐	☒	☐
Boehringer Ingeiheim	Advisory Board and Honoraria	☐	☒	☐	☐
Bristol-Myers Squibb	Advisory Board and Honoraria	☐	☒	☐	☐
Eisai	Advisory Board and Honoraria	☒	☐	☐	☐
Merck	Advisory Board and Honoraria	☐	☐	☒	☐
Novartis	Advisory Board and Honoraria	☐	☒	☐	☐
Pfizer	Advisory Board and Honoraria	☐	☒	☐	☐
Roche	Advisory Board and Honoraria	☐	☒	☐	☐
Astra Zeneca	Research Funding	☐	☐	☐	☒
Bristol-Myers Squibb	Educational Grant	☒	☐	☐	☐

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 15

Name: Dr. Ronald Burkes

Position: Medical oncologist, Mount Sinai Health
Date: Sept 12, 2022

☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 5: Conflict of Interest Declaration for Clinician 15

	Check appropriate dollar range*			
Company	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
NA				

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 16

Name: Dr. Shaqil Kassam
Position: Medical Oncologist, Southlake Regional Hospital
Date: Sept 12, 2022

☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 5: Conflict of Interest Declaration for Clinician 16

	Check appropriate dollar range*			
Company	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
Roche	x			
Merck	x			
BMS	x			
Takeda	x			
Novartis	x			
Ipsen	x			
Sanofi	x			
Pfizer	x			

* Place an X in the appropriate dollar range cells for each company.

Declaration for Clinician 17

Name: Dr. Kevin Jao
Position: Medical Oncologist, Hôpital Sacré-Cœur, Montreal
Date: Sept 12, 2022

☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 5: Conflict of Interest Declaration for Clinician 17

Bristol-Myers Squibb	Nature or description of activities or interests	Check Appropriate Dollar Range			
		$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Bristol-Myers Squibb	Advisory Role	☒	☐	☐	☐

Declaration for Clinician 18

Name: Dr. Barb Melosky
Position: Medical Oncologist, BC Cancer
Date: Sept 12, 2022

☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 5: Conflict of Interest Declaration for Clinician 18

Company	Nature or description of activities or interests	Check Appropriate Dollar Range			
		$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Novartis	Advisory Board	☒	☐	☐	☐
Roche	Advisory Board	☒	☐	☐	☐
Merck	Advisory Board	☒	☐	☐	☐

Declaration for Clinician 19

Name: Dr. Parneet Cheema
Position: Medical Director of Cancer Care, William Osler Health System
Date: Sept 12, 2022

☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 5: Conflict of Interest Declaration for Clinician 19

Company	Nature or description of activities or interests	Check Appropriate Dollar Range			
		$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
Bristol Myers Squibb	Advisory board/Honoraria	☒	☐	☐	☐
Merck	Advisory board/Honoraria	☒	☐	☐	☐
Astrazeneca	Advisory board/Honoraria	☒	☐	☐	☐
Roche	Advisory board/Honoraria	☒	☐	☐	☐
Novartis	Advisory board/Honoraria	☒	☐	☐	☐

Declaration for Clinician 20

Name: Dr. Mahmoud Abdelsalam
Position: Medical Oncologist, Horizon Health Network
Date: Sept 12, 2022

☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 5: Conflict of Interest Declaration for Clinician 20

Company	Nature or description of activities or interests	Check Appropriate Dollar Range			
		$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
BMS	Advisory role, Honoraria and travel grants	☐	☒	☐	☐

Declaration for Clinician 21

Name: Dr. David Stewart
Position: Medical Oncologist, The Ottawa Hospital
Date: Sept 12, 2022

☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 5: Conflict of Interest Declaration for Clinician 21

Company	Nature or description of activities or interests	Check Appropriate Dollar Range			
		$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
NA			☐	☐	☐

Declaration for Clinician 22

Name: Dr. Nathalie Daaboul
Position: Hemato-oncologist, Charles-Le Moyne Hospital, Université de Sherbrooke
Date: Sept 12, 2022

☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 5: Conflict of Interest Declaration for Clinician 22

Company	Nature or description of activities or interests	Check Appropriate Dollar Range			
		$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
NA			☐	☐	☐

Declaration for Clinician 23

Name: Dr. Mark Vincent
Position: Medical Oncologist, London Regional Cancer Centre
Date: Sept 12, 2022

☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 5: Conflict of Interest Declaration for Clinician 23

Company	Nature or description of activities or interests	Check Appropriate Dollar Range			
		$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
NA			☐	☐	☐

Declaration for Clinician 24

Name: Dr. Jawaid Younus
Position: Medical Oncologist, London Regional Cancer Centre
Date: Sept 12, 2022

☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 5: Conflict of Interest Declaration for Clinician 24

Company	Nature or description of activities or interests	Check Appropriate Dollar Range			
		$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
NA			☐	☐	☐

Declaration for Clinician 25

Name: Dr. Diana Ionescu
Position: Consultant Pathologist, BC Cancer Agency
Date: Sept 12, 2022

☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 5: Conflict of Interest Declaration for Clinician 25

Company	Nature or description of activities or interests	Check Appropriate Dollar Range			
		$0 to 5,000	$5,001 to 10,000	$10,001 to 50,000	In Excess of $50,000
NA			☐	☐	☐

Declaration for Clinician 26

Name: Dr. Silvana Spadafora
Position: Medical Oncologist, Sault Area Hospital
Date: Sept 12, 2022

☒ I hereby certify that I have the authority to disclose all relevant information with respect to any matter involving this clinician or clinician group with a company, organization, or entity that may place this clinician or clinician group in a real, potential, or perceived conflict of interest situation.

Table 5: Conflict of Interest Declaration for Clinician 16

Company	Check appropriate dollar range*			
	$0 to $5,000	$5,001 to $10,000	$10,001 to $50,000	In excess of $50,000
NA				

* Place an X in the appropriate dollar range cells for each company.