## CADTH REIMBURSEMENT REVIEW

# Patient and Clinician Group Input

**fruquintinib (TBC)**

(Takeda Canada Inc.)

**Indication:** For the treatment of adult patients with metastatic colorectal cancer (mCRC) who have been previously treated with or are not considered candidates for available therapies, including fluoropyrimidine-, oxaliplatin-, and irinotecan-based chemotherapy, an anti-VEGF therapy, and an anti-EGFR therapy.

**May 21, 2024**

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 Group Input

## Colorectal Cancer Canada

Name of Drug: fruquintinib

Indication: metastatic colorectal cancer (mCRC)

Name of Patient Group: Colorectal Cancer Canada

Author of Submission: Iris Karry

### About Colorectal Cancer Canada

Colorectal Cancer Canada is the nation's not for profit colorectal cancer patient organization dedicated to colorectal cancer awareness and education, supporting patients and their caregivers and advocating on their behalf.

Colorectal Cancer Canada is registered with CADTH.
www.colorectalcancercanada.com

### Information Gathering

To capture the patient perspective, Colorectal Cancer Canada (CCC) conducted interviews via Zoom between April 1st and May 15th, 2024 with patients in the United States and Canada (Patients 1-4). Patients 1-3 had experience with fruquintinib. Data from an online survey circulated by CCC in August 2023 for a previous CADTH submission (Patients 5-19, Caregiver 1) were also used to provide data for sections 3, 4, 5.

### Table #1: Demographics of Interviewees

| | Patient 1 | Patient 2 | Patient 3 | Patient 4 |
|---|---|---|---|---|
| **Country, Province/State** | United States, Florida | United States, Michigan | United States, Oklahoma | Canada, Quebec |
| **Gender, Age** | Female, 41-50 years | Male, 41-50 years | Female, 31-40 years | Male, 51-60 years |
| **Stage at Diagnosis** | III | III | III | III |

### Table 2: Demographics of Patients and Caregiver Surveyed

| | Patient 5 | Patient 6 | Patient 7 | Patient 8 | Patient 9 | Patient 10 |
|---|---|---|---|---|---|---|
| **Country and Region** | Nova Scotia, Canada | Quebec, Canada | Quebec, Canada | British Columbia, Canada | Ontario, Canada | Quebec, Canada |
| **Gender, Age** | Female, 61-70 years | Female, 51-60 years | Male, 41-50 years | Female, 61-70 years | Female, 31-40 years | Female, 31-40 years |
| **Stage at Diagnosis** | IV | IV | IV | III | IV | IV |

| | Patient 11 | Patient 12 | Patient 13 | Patient 14 | Patient 15 | Patient 16 |
|---|---|---|---|---|---|---|
| **Country and Region** | Newfoundland & Labrador, Canada | Quebec, Canada | Nova Scotia, Canada | Quebec, Canada | British Columbia, Canada | Alberta, Canada |
| **Gender, Age** | Male, 61-70 years | Female, 41-50 years | Female, 31-40 years | Gender unspecified, 61-70 years | Female, 61-70 years | Female, 51-60 years |
| **Stage at Diagnosis** | IV | III | IV | Unsure | IV | IV |
| | Patient 17 | Patient 18 | Patient 19 | Caregiver 1 | | |
| **Country and Region** | Prince Edward Island, Canada | Quebec, Canada | Quebec, Canada | British Columbia, Canada | | |
| **Gender, Age** | Female, 51-60 years | Male, 51-60 years | Male, 61-70 years | Female, 51-60 years | | |
| **Stage at Diagnosis** | III | IV | IV | IV | | |

## Disease Experience

***Survey data regarding disease experience is summarized in the PDF attached, entitled: "Summary graphs – Disease* Experience".**

Patients and caregivers were asked about which symptoms of colorectal cancer (CRC) they experienced (Q9). 94% of respondents experienced CRC symptoms (Q8), with bloody stools, abdominal pain, fatigue and weakness cited as the most common symptoms. When asked what the top CRC symptoms were the most important to control (Q10), respondents selected fatigue and weakness, abdominal pain, anemia, and diarrhea. 13 out of 16 patients/caregivers indicated that their CRC symptoms directly and/or indirectly limited their quality of life (Q11). Respondents were asked to select the three most important ways the CRC symptoms they experienced impacted their quality of life, with ability to work, ability to exercise, and ability to participate in social activities cited as the most important.

When asked about the psychological impact of CRC (Q12), patients cited persistent fear of [the] cancer getting worse or recurring (coming back); feeling consistently worried, nervous or uneasy; persistent fear of hopelessness about [the] future; and inability to concentrate or perform activities that require mental acuity as the most common impacts. Patient 6 expanded on the impact of CRC in their interview: "*The part that impacts my life more is not the question of whether I will die, but rather, how my life at the moment is limited. I can't travel, I can't plan more than 3 weeks ahead. I feel like I am wearing handcuffs".*

Patient 4 commented on the psychological turmoil he faced after his diagnosis with CRC: "*You start with the diagnosis, and you face the fact that you may die. Then you undergo surgery, and the medical team tells you that maybe can be cured. Then you have a recurrence, and now you are in stage IV. Then you think, ok now I really think I will die. The doctors tell you no, you are still operable. Grasping at all of these things, you are on a psychological rollercoaster. Then you get to the point where everything available has failed. It is extremely psychologically trying.*"

Caregivers were uniquely questioned on the difficulties they faced while caring for the individual living with CRC (Q36-39). The one caregiver who responded to the survey indicated that the main difficulties they faced were: inability to plan for the future, time spent at medical appointments, difficulty managing treatment-induced side effects or symptoms of the cancer, feeling helpless or inadequate, and physical/emotional exhaustion (caregiver burnout). They indicated that an average of 0-10 hours were dedicated per week to managing the patient's side effects, and an average of 0-10 hours a week were dedicated to managing the patient's treatment including taking them to appointments, administration of medication, and hospital/clinic visits.

The following open-ended responses were provided regarding the difficulties they faced:

- "*Managing time to attend appts and treatments, feeling helpless when the patient cannot eat or is unable to do their regular activities, so I have to take over those activities along with managing my daily chores. "*
- *"Had to go part time. Financial challenges. Worry, anxiety, depression*."

## Experiences With Currently Available Treatments

***Survey data regarding experience with currently available treatments is summarized in the PDF attached, entitled:*** **"Summary graphs – Experiences with Currently Available Treatments".**

Patients and caregivers were asked to indicate which drug therapies they have accessed to treat their CRC (Q19). FOLFOX, FOLFIRI, capecitabine, and panitumumab were cited most frequently. Fatigue, diarrhea, hair loss and nausea were cited as the most common side effects experienced with drug therapies (Q24), while the most difficult side effects to tolerate were neuropathy, nausea and fatigue (Q26). Patients/caregivers were asked whether they experienced any difficulties during the administration of a treatment (Q20). 8 patients responded, with 4 patients indicating that they experienced no difficulties. From the 4 other respondents, the following open-ended responses were provided:

- *"Yes. Difficulties swallowing, difficulties with Port-o-cath installation. Problems with displacement of Port-o-cath in heart. Hepatic Arterial Infusion challenges with dosage and abdominal pain; pain in my hands"*
- *"Vomiting during infusion, chemo delays due to blood parameters being too low."*
- *"First port-o-cath blocked with fibrin clot three weeks after implantation. A second one had to be placed."*
- *"Mechanical issues with 5-FU pump*"

When asked whether these drug therapies have been effective at controlling the symptoms of the cancer, such as pain (Q21), 15% of patients/caregivers said "no", 31% said "somewhat", and 54% said "yes". When asked whether

these drug therapies have been effective at controlling the progression of the disease (Q22), 8% said "no", 25% said "somewhat", and 67% said "yes", with the following open-ended responses:

- *"They allowed me to reduce tumour burden and have the cancer removed from the colon, liver and lungs"*
- *"Was able to proceed with surgery since I had a response to chemo, therefore I became a surgical candidate"*

Respondents also indicated (Q23) that they accessed other therapies such surgery and radiofrequency ablation to treat their cancer. Patients/caregivers were asked if they experienced any difficulties accessing drugs for their colorectal cancer (Q28), to which the following open-ended responses were provided:

- *"Had to leave the country for some of the treatments. (HAI)"*
- *"My Avastin has now been defunded by BC Cancer and I don't have extended coverage and so far no one has been able to tell me the cost so I can know if I can afford it"*

Patients/caregivers were asked to rate on a scale of 1-10 (1 being "not important", 10 being "very important") the importance of access to new, effective therapies for CRC (Q14). 93% of respondents indicated that access to such therapies was very important to them. When patients/caregivers were asked whether they believed their needs are not being met by current drugs available to treat their cancer (Q35), 39% replied "yes", with the following open-ended responses:

- *"Options seem more diversified in the U.S."*
- *"Just back from my oncologist and the Lonsurf and Avastin is not working. I have new growth and growth on existing tumours. I have ascites now too. KRAS mutation as well. I'm running out of options."*
- *"Need options beyond FOLFOX and FOLFIRI"*
- *"Need more information about what is available I am only told there is a protocol for my stage of cancer, and treatment is determined by BC Cancer*".

CCC conducted four interviews with patients, three of which reside in the US and one in Canada. All were diagnosed with stage III CRC and treated with the standard arsenal of surgery and combination chemotherapies. Despite initial responses to treatment, all experienced significant tumour progression on standard therapies which resulted in the need to access a broader array of therapies. Their experiences highlight the stark limitations of currently available therapies and the important unmet need experienced by patients in the metastatic setting for more effective treatment options to stabilize their disease and maintain/improve their QOL.

Patient 1 was diagnosed with stage III CRC at age 42. The cancer was initially treated with surgery and FOLFOX. After one year, the cancer recurred in the liver and the patient was diagnosed with stage IV disease. The patient underwent a liver resection, radiation, and received FOLFOX and FOLFIRI. She lost her hair due to treatment, experienced severe neuropathy, was constantly exhausted, and had to stop working. As a young mother, she struggled to keep up with her 3-year-old son and manage her daily activities. Just as she began to feel better after a cycle of chemotherapy, it was time for another round. The chemotherapy elicited modest responses in her tumours. Given the challenges she faced with side effects from standard treatments and the limitations of current options to

manage disease progression, she actively sought out a clinical trial with fruquintinib in hope of exploring more effective alternatives.

Patient 2 was diagnosed with stage III CRC that was initially treated with surgery and FOLFOX. The patient was NED for one year until the cancer recurred, resulting in a diagnosis of stage IV disease. Due to the complicated location of recurrence in the retroperitoneal lymph nodes, surgery was not an option due to proximity to major arteries. The patient was treated with FOLFIRI, which produced modest responses in his tumours. Eventually the tumours shrunk enough for the patient to be able to undergo cytoreductive surgery after seeking out a surgeon specialized in the retroperitoneal region. The surgery helped to control the disease for some time. Eventually the cancer progressed again, at which time the patient was referred to a clinical trial with fruquintinib.

Patient 3 was diagnosed with stage III CRC that was initially treated with chemotherapy. Within 8 weeks, spots were found on her liver and she underwent liver resection. She remained on capecitabine chemotherapy. At a subsequent scan, spots were found on her lungs. She received FOLFOX but had a bad reaction to it and was placed on FOLFIRI. At a subsequent scan, spots were found in her ovary and abdomen, with several new spots in her lung. The patient was referred to a clinical trial with fruquintinib.

Patient 4 was diagnosed with stage III CRC in 2014. He underwent 6 months of CAPOX and was NED for approximately 1 year. The CAPOX caused terrible nausea and hand-foot syndrome. At a routine follow-up, a recurrence was found in the peritoneum and the patient was diagnosed with stage IV disease. He underwent CRS-HIPEC and surgery to remove a recurrence in the sigmoid colon, which resulted in a temporary ostomy. In early 2017, the patient underwent a second-line of chemotherapy – FOLFIRI – for 3 months. He was NED for several months until he noticed a pain in his right leg. Scans showed a significant recurrence in the colon, liver, lung, bone, and peritoneum. He was unable to walk and participate in many daily tasks. The patient enrolled in a clinical trial and received pembrolizumab and binimetinib, but due to a severe reaction to the latter, had to leave the trial. In late 2018 the patient received Lonsurf but due to a severe adverse reaction, had to stop taking the drug. The patient eventually went to the United States for a second opinion consult and received ipilumumab-nivolumab off-label. The patient experienced excruciating pain, was taken off of ipilimumab and was prescribed strong opioids. Eventually the pain started improving and at his next scan the medical team said that the tumours were shrinking everywhere. Ultimately, he had to stop taking nivolumab because he went into adrenal crisis. In 2021, the patient underwent a total colectomy which resulted in a permanent ostomy. From that point until today, scans show that he is NED. The patient currently lives with chronic neuropathy, a permanent ostomy, and long-term side effects of opioid use including sleep disturbances. Furthermore, to access additional treatment options, the patient spent between $200,000-$250,000 in out-of- pocket costs, highlighting the extremely high cost to accessing additional therapeutic options once standard of care options in Canada had been exhausted.

## Improved Outcomes

***Survey data regarding improved outcomes is summarized in the PDF attached, entitled: "Summary graphs – Improved* Outcomes".**

Patients/caregivers were asked to rate how important it is to them for a new therapy to bring about improvement to their physical condition and quality of life (Q40 and Q41). 67% of respondents replied that it is very important for a new therapy to bring about improvement to their physical condition (e.g. tumour shrinkage, tumour stability,

reduction of pain) and 64% of respondents indicated that it was very important for a new therapy to bring about improvement in their quality of life. 100% of respondents indicated that they would be willing to take a drug that has been proven to provide better quality of life even if it does not extend overall survival (Q42).

## Experience With Drug Under Review

**Patient 1**

In 2019, Patient 1 was diagnosed with stage III CRC at age 42 and underwent the standard treatment of surgery and FOLFOX. Her cancer recurred one year later in the liver and lymph nodes. Following a liver resection and further rounds of FOLFOX and FOLFIRI which produced side effects including fatigue and neuropathy that were very difficult to manage, she personally sought out a clinical trial with fruquintinib and was enrolled in September 2022. She pays out of pocket for her travel costs from Florida to Tennessee once a month to get to the trial centre. Luckily, she has a friend in Nashville who she stays with and therefore does not incur lodging fees. Treatment costs and scans are covered by the trial, while her insurance covers the costs of additional medications she takes to manage side effects.

Patient 1 states that the quality of life (QOL) improvement on fruquintinib has been significant - "*when you feel good, you want to do more things*", and indicates how she has been able to return to many of her daily activities and "*live a pretty normal life*". Since she began taking fruquintinib, she stated that it has been "*absolutely amazing…shocking…at my last scan, the cancer was barely visible, and this far down the road (1 year and 6 months), the drug is still working*." In terms of administering the drug, Patient 1 indicated that she has no issues taking the pills and felt a lot more flexibility with her treatment as she can administer the drug at home. Comparing fruquintinib to chemotherapy, she stated that the latter "*was mentally draining. You have to sit in an infusion chair for hours and plan your life around it. With fruquintinib, you can take the pills at home and build it into your schedule. You have so much more time!*

*Time with your family*."

While she was initially placed on the 5mg dose of fruquintinib, she had to lower her dose in the summer of 2023 to 4mg and is currently on 3mg which seems to be the most tolerable for her while still producing results. The most significant side effects she has experienced are Hand-Foot syndrome, which produced very severe pain (pain level 10, on a scale of 1-10) in her feet. When she reduced her dose, the intensity of pain was alleviated. Patient 1 also experienced thyroid issues and pancreatitis due to fruquintinib, but both were managed with medication.

While taking fruquintinib, Patient 1 was able to start working again, go back to exercising, travelling, taking care of her son, and going to his baseball games, cleaning the house and doing all her usual daily activities. With fruquintinib, she stated that she "*has her autonomy back*" and feels *almost* back to where she was before she was diagnosed with CRC.

**Patient 2**

Patient 2 was diagnosed with stage III CRC at age 41 in late 2018 and underwent the standard treatment of surgery and FOLFOX. He was NED until early 2020 when he was diagnosed with stage IV CRC after a recurrence. After additional surgery that was unable to successfully remove the affected lymph nodes due to their precarious location adjacent to major blood vessels, Patient 2 continued on FOLFIRI in addition to a co-factor drug that he accessed

through a clinical trial. His cancer responded well to the treatment and the tumours decreased enough for a surgeon more skilled in the retroperitoneal region to remove the affected lymph nodes. The cancer stabilized for some time before it progressed. In August of 2022, Patient 2 enrolled in a clinical trial to receive fruquintinib in combination with the PD-1 inhibitor tislelizumab. From Michigan, he flew down to Tennessee once a month to the trial centre. Through the trial he was able to receive partial funding for his travel costs, and the rest he was able to get covered through a separate funding organization.

Patient 2 experienced severe fatigue, bad diarrhea, and hypertension while on fruquintinib and tislelizumab but was able to manage most of his side effects well with medications. He stated that "*fruquintinib is not the easiest drug in the world, but it is WAY better than chemo*." He experienced Hand-Foot syndrome but was able to control it with a good over-the-counter lotion. Patient 2 indicated

that fruquintinib helped to stabilize his cancer – "*fruquinitnib is not going to cure your cancer, but some stuff shrunk, and there was no more major growth*". In total, he received fruquintinib for 14 months and he was able to "*feel normal again*" and "*I could take the drug and go out to dinner*", stating he could also do longer trips with his family and generally enjoy his life more. Comparing fruquintinib to his experience with chemotherapy, Patient 2 indicated that "*it takes 3-4 days to feel better after chemo, and you really cannot move around much and travel when you are taking it. Your life revolves around when you will be receiving it next*." Despite positive overall results while receiving fruquintinib and tislelizumab, eventually Patient 2 had to leave the trial because he experienced some tumour growth that partially obstructed his bile duct, which was considered a progression. He has returned to chemotherapy which has been producing good results to date as rechallenge therapy.

**Patient 3**

Patient 3 was diagnosed with stage III CRC at age 39 in 2017. She underwent capecitabine chemotherapy but at her next scan, spots were found in her liver. She underwent a liver resection and remained on capecitabine. At her next scan, spots were found in her lungs. She received FOLFOX but had a bad reaction to oxaliplatin and was given FOLFIRI. At a subsequent scan, spots were found in her ovary and abdomen, with several new spots in her lung. She was referred to a clinical trial for fruquintinib in combination with tislelizumab. While on the combination, Patient 3 experienced hypertension, which was controlled with medication. She also experienced Hand-Foot syndrome, but having been on capecitabine for years she was familiar with the side effect and was able to manage it well. She remained on the 5mg dose of fruquintinib throughout the trial. At her first scans after starting fruquintinib, there was shrinkage in her tumours and her CEA levels had diminished. While her cancer was not cured, her cancer was stabilizing. She was able to "*live life normally*" and the drug "*gave her more time. Chemo works at first, but it does not work for a long time*."

Patient 3 had all treatment costs covered by the clinical trial. She describes how she had no issues with the treatment regimen, and experienced greater flexibility compared to chemotherapy. With chemotherapy, she describes: "*the more you take, the harder it gets. It would take 3-7 days to recover, and as soon as I started feeling better it would be time to get hooked back up again. With fruquintinib, it felt like you just managing a chronic disease, and you can take the medication with you*."

**Summary Statement**

Access to fruquintinib for patients in the refractory, metastatic CRC setting is of utmost importance because it provides patients in this subgroup with an effective treatment option to stabilize their disease and improve their QOL. Fruquintinib allowed patients to return to a feeling of normalcy in their lives, regain a sense of autonomy, and enjoy more flexibility in their day-to-day life. Although the treatment did come with some significant side effects, the majority were able to be managed well through medications.

## Companion Diagnostic Test

None.

## Anything Else?

There is a significant unmet need for additional treatment options for patients in the refractory metastatic setting. While several treatment options have become available in this setting in recent years, there are inequities in access across Canada. Furthermore, there are patients who may not be eligible for, may respond poorly to, or be forced to stop currently available treatments due to severe adverse events and therefore require additional, effective options to be available. **We, therefore, strongly support and urge that a positive funding recommendation be issued for fruquintinib for the treatment of metastatic colorectal cancer.** We believe this drug aligns well with the identified patient need for an effective treatment option that is capable of prolonging life and maintaining/improving QOL.

## Appendix: Colorectal Cancer Canada Conflict of Interest Declaration

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

No.

**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.

**List any companies or organizations that have provided your group with financial payment over the past 2 years AND who may have direct or indirect interest in the drug under review.**

### Table 1: Financial Disclosures

**1.1 Check Appropriate Dollar Range With an X. Add additional rows if necessary.**

| Company | $0 to 5,000 | $5,001 to 10,000 | $10,001 to 50,000 | In Excess of $50,000 |
|---|---|---|---|---|
| Abbvie Corp. | | | X | |
| Amgen Canada Inc. | | | | X |
| Astra Zeneca Canada Inc. | | | | X |
| Bayer Inc. | | | | X |
| Boehringer Ingelheim Ltd. | | | | X |
| Hoffmann-La Roche | | | | X |
| Innovative Medicines Canada | | | | X |
| INCYTE | | | X | |
| Janssen Inc. | | | | X |
| Pfizer Canada Inc. | | | | X |
| Taiho Pharma Canada | | | X | |
| GlaxoSmithKline | | | | X |
| Novartis | | | X | |
| Merck Canada Inc. | | | | X |
| Bristol Myers Squibb Canada | | | | 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:** Iris Karry

**Position:** Manager, Patient Education & Research

**Patient Group:** Colorectal Cancer Canada

**Date**: 21/05/2024

## Colorectal Cancer Resource & Action Network (CCRAN)

| | |
|---|---|
| **Name of the Drug and Indication** | **Fruquintinib: For the treatment of adult patients with metastatic colorectal cancer (mCRC) who have been previously treated with or are not considered candidates for available therapies, including fluoropyrimidine-, oxaliplatin-, and irinotecan-based chemotherapy, an anti-VEGF therapy, and an anti-EGFR therapy.** |
| **Name of the Patient Group** | **Colorectal Cancer Resource & Action Network (CCRAN)** |
| **Author of the Submission** | **Filomena Servidio-Italiano, CCRAN** |
| **Name of the Primary Contact for This Submission** | **Filomena Servidio-Italiano, President & CEO, CCRAN** |
| Email | [redacted] |
| Telephone Number | [redacted] |

### About Colorectal Cancer Resource & Action Network (CCRAN)

**CCRAN** is a national, not-for-profit patient advocacy group championing the health and wellbeing of Canadians touched by colorectal cancer and others at risk of developing the disease, by providing support, education and advocacy to help improve patient outcomes by way of longevity and quality of life. We have expanded our mandate to serve cancer patients outside of the colorectal cancer space through HTA patient evidence submissions, educational events and advocacy initiatives. Our mission is to reduce the burden of cancer in Canada. (www.ccran.org)

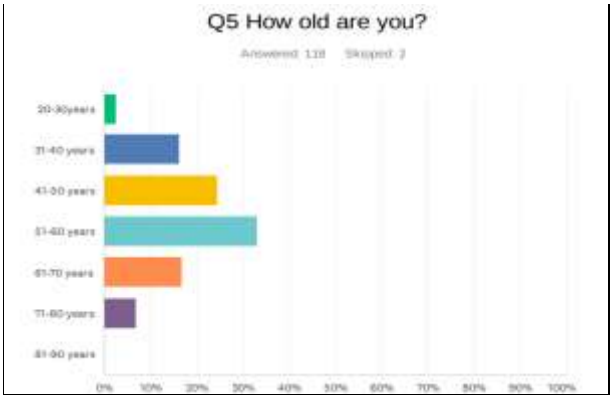
### Information Gathering

To ensure the metastatic colorectal cancer patient perspective was captured for this therapeutic under review, CCRAN employed a multi-faceted outreach approach. On February 25, 2024, CCRAN reached out to 10 United States-based (U.S.-based) Clinicians (via email) who treat metastatic colorectal cancer patients requesting their assistance in helping to identify patients (or caregivers) who had/have experience with Fruquintinib therapy for the purposes of participating in a telephone interview. Patients or caregivers were being asked to share their lived experience not only for the therapy under review, but, their cancer journey and previously accessed therapies as well, to help inform our HTA patient input submission. To encourage accrual, we attached a patient flyer (**APPENDIX 2)** to the clinician email which we requested be shared with patients who had experience with Fruquintinib. Follow-ups were then sent at the three and five week point. Recognizing this would be a challenging submission with respect to securing the patient's lived experience with Fruquintinib in Canada, and the U.S., CCRAN also reached out to U.S.-based patient advocacy groups to request their assistance with patient accrual for telephone interviews: Fight Colorectal Cancer, Colorectal Cancer Alliance and G.I. Cancers Alliance (**February 25th, 2024**). The same patient flyer was shared with the heads of the patient advocacy groups. A follow up email was sent at the two and four week mark. Three high quality patient interviews resulted from our clinician and patient advocacy group outreach, all of whom are U.S.-based, whose qualitative data is captured and summarized in **APPENDIX 1**. The current mean

and median age of the interviewed patients is 43.3 years and 47 years respectively; and the mean and median age at their time of diagnosis was 38 and 41 years respectively. All interviewed patients were early onset colorectal cancer patients, which underscores the disturbing rising rates of the pathology in the under 50 year old patient population.

An online survey (targeting metastatic colorectal cancer patients only – **APPENDIX 3**) was developed and disseminated throughout Canada from March 21st – April 17th 2024 gauging the patient's lived experience with respect to their cancer diagnosis, cancer journey, drug therapies administered prior to having received the therapy under review, and the lived experience with respect to Fruquintinib. The online survey was promoted through CCRAN's email blasts, social media channels and monthly support groups. 119 respondents completed the survey, 115 resided in Canada and the balance of whom were from the U.S. 107 respondents confirmed they (or their loved one) had been diagnosed with stage IV disease (**Q6**).

All provinces were represented with the exception of Prince Edward Island and the Territories. (**Q3**). From the 115 Canadian respondents, **84** responded as patients, **28** as caregivers and **2** responded as patients who were also caregivers (**Q7**) which totaled 114. Twice as many women (79) responded to the survey than did their male counterparts (35) (**Q4**).




Adults between the ages of 20 and 80 years are well represented in the survey findings (**Q5**), with **43%** of respondents appearing in the under 50 years patient population.

For those patients who responded in the 51-60 year category, a number of them were likely diagnosed as early age onset patients as well (<50 years of age), once again underscoring the importance in the rising rates of this pathology in the

In addition to the 3 interviewed patients, two surveyed patients provided their lived experience with Fruquintinib therapy. In total, 5 patients have provided their lived experience with respect to Fruquintinib for this submission. The qualitative data provided through the telephone interviews will serve for the most part as the basis for this submission, in addition to the objective online survey findings to support the use of Fruquintinib therapy.

## Disease Experience

Colorectal cancer is the third most commonly diagnosed cancer and the second leading cause of cancer-related death in Canada. Approximately 50% of patients with colorectal cancer develop distant metastases during their disease course and the long term survival rate continues to be poor for this patient population. This highlights the need for additional therapeutics to improve longevity and quality of life for these patients.

Our online survey results (APPENDIX 3) were quite revealing: **87.3%** of our surveyed respondents experienced colorectal cancer symptoms (**Q8**). The results identified **fatigue, abdominal cramping and bloody stools** as the most prevalent colorectal cancer-induced symptoms (**Q9**) and not surprisingly, **fatigue**, which resulted from the cancer, was the most important symptom to control, according to the patients and caregivers (**Q10**). In **Q11**, patients relayed that their colorectal cancer-induced symptoms most certainly interfere with their quality of life (QoL) and their daily activities: **77%** are unable to work and **62%** are unable to exercise, while **45%** are unable to fulfill their family obligations, while **40%** are unable to concentrate. These are daily functions/abilities/tasks that prevent patients from leading a normal life, from leading the lives to which they have grown accustomed and from which they derive fulfillment and joy. These are limitations that are imposed upon patients resulting directly from their cancer. Limitations that rob them of that previously referred to joy and fulfillment as made evident from some of the open-ended replies (**Q12**):

- "***I can't plan travel or socials because of side effects***"
- "***Not intimate with my husband***"

The top three limitations that had a psychological impact from patients' colorectal cancer (**Q12**) were:

- Inability to plan for the future or think about the future (75%)
- Constant fatigue makes it difficult to function normally – can't think straight (49%) and Chemo brain makes me feel forgetful, "less than" (49%)
- Inability to experience joy (30%) and Can't see myself getting better (30%)

Not all colorectal cancer patients experience symptoms from their cancer. Approximately **12%** of the survey respondents did not experience any cancer-induced symptoms prior to receiving their colorectal cancer diagnosis. And two of the three interviewed patients had not experienced any cancer-induced symptoms prior to receiving their diagnosis either. **Patient A** (**APPENDIX 1**) discovered she had been anemic for approximately 5 years prior to her diagnosis, which was a sign of colorectal cancer but she had not been advised of the correlation between low hemoglobin and the onset of colorectal cancer. **Patient C** underwent bloodwork which incidentally detected his anemia and was recommended to undergo a colonoscopy which then identified his colon cancer. **Patient B** was the only patient who had been experiencing cancer-induced symptoms (abdominal pain) for approximately 3 months prior to her diagnosis which eventually necessitated an Emergency Department visit and the delivery of a stage IV colorectal cancer diagnosis requiring immediate surgical resection of her colon.

Interviewed patients expressed how emotionally distraught they were when delivered a diagnosis of colorectal cancer (**Q7E**). They were forced to immediately start navigating a world that was completely unknown to them and a cancer that was deemed to be fatal at their young age:

**Patient A shared**:
***"…I was very upset because it does not run in my family. I was in shock. I did not have time to digest this, I went into surgery in 6 days. I just didn't have time to understand how sick I was. Everything happened very quickly for me, surgery, chemo, surgery, then chemo then NED….then stage 4 disease…I had to be put on antidepressants***."

**Patient B:**
"***Absolutely devastated. Because I was horrified and it broke my heart. I couldn't bare it... (*started to cry***). I was so young…."***

**Patient C:**
"***Oh my God, I felt terrible….my doc told me I was done doing what I did. That was the most devastating news. Then I found out we were pregnant and I wanted to be around for her. I had this huge elephant in the room. I tried to be as positive as I can. I tried to research cancer and become a good father. It's so hard…"***

As for the toll the disease has taken on caregivers, **Q36** results identified the following top three difficulties caregivers face in caring for loved ones with colorectal cancer:

- Loss of lifestyle (74%)
- Difficulty managing treatment induced side effects (66%)
- Loss of income (55%)

These challenges merely underscore the impact of the disease on the caregiver as they struggle with the emotional, physical and financial turmoil of the diagnosis, but as one survey respondent states, "***Difficulty researching and accessing potential treatments***" is a considerable ongoing challenge imposed upon the caregiver from which there is little to no reprieve. (**Q36**) Other open-ended replies included:
"***Seeing husband in pain and chemo for life attitude by oncology and advocating for other options and surgery etc. other information I'm constantly researching and can't stop thinking I have to save him because oncology mindset is chemo only***."
"***Managing effects on our young children."***
These are two critically important perspectives that resonate repeatedly throughout the survey findings and throughout the interview data for reasons alluded to previously: colorectal cancer is on the rise in Canadians under the age of 50. Our interviewed patients are under the age of 50 and a significant number of survey respondents are also early age onset patients who were diagnosed while raising young families, having embarked on promising careers as contributing members of society. A diagnosis of metastatic colorectal cancer is robbing these patients of not only their quality of life but a productive and fulfilling life with their young families which necessitates aggressive and concerted efforts and advocacy to ensure access to promising and effective therapies to help improve patient outcomes.

## Experiences With Currently Available Treatments

Metastatic colorectal cancer patients who completed the online survey (**Q16**) received treatment with fluorouracil-based chemotherapy (with oxaliplatin – **61.97%** and irinotecan – **71.83%**), vascular endothelial growth factor (VEGF)-based therapy (mainly bevacizumab – **57.75%**), and epidermal growth factor receptor

(EGFR)-targeted therapies in confirmed RAS wild type disease (either Cetuximab or Panitumumab – **1.41%** and **15.49%** respectively). **30.99%** accessed Capecitabine; Pembrolizumab was accessed by **5.63%** of the survey respondents while Encorafenib in combination with an anti-EGFR therapy was accessed by **4.23%** of the survey respondents. **4.23%** accessed Lonsurf monotherapy and an additional **4.23%** accessed Lonsurf + bevacizumab. Open ended replies revealed additional systemic therapies were accessed which included: Nivolumab in combination with Ipilimumab, Amivantamab monotherapy, and Raltitrexed.

Based on these treatments accessed, patients cited **fatigue**, **hair loss**, **nausea**, **peripheral neuropathy,** and **diarrhea** as the most commonly induced side effects from their colorectal cancer therapies (**Q18**). The three treatment-induced side effects that were most difficult to tolerate as identified in the survey findings (**Q20**) were fatigue (**48.3%**), nausea (**41.6%**), and diarrhea (**21.6%**).

Patients rated the impact of their treatment-induced side effects from "***No Impact***" to "***Significantly Impacting***" their daily life, the results of which appear below:

| | NO IMPACT | SMALL IMPACT | MODERATE IMPACT | SIGNIFICANT IMPACT | TOTAL | WEIGHTED AVERAGE |
|---|---|---|---|---|---|---|
| Side Effect #1: | 1.52% 1 | 7.58% 5 | 21.21% 14 | 69.70% 46 | 66 | 3.59 |
| Side Effect #2: | 1.56% 1 | 9.38% 6 | 29.69% 19 | 59.38% 38 | 64 | 3.47 |
| Side Effect #3: | 1.64% 1 | 4.92% 3 | 54.10% 33 | 39.34% 24 | 61 | 3.31 |

The **three weighted averages** appearing above (**3.59, 3.47 and 3.31)** each reflect the profound impact the treatment-induced side effects had/have on the patients' daily lives and quality of life, regardless of the side effects selected: the majority of the respondents selected "**significant impact**" for **Side Effect #1** and the majority then proceeded to select either "**significant impact**" and/or "**moderate impact**" for **Side Effect #2** and **Side Effect #3**.

To help address the treatment-induced side effects and improve patients' quality of life, patients were prescribed medications which included (**Q22**):

**Nausea**: ondansetron, metoclopramide, prochlorazine, meclizine, Zofran, Emend, Aprepitant
**Fatigue**: dexamethasone
**Constipation**: laxatives and stool softeners
**Diarrhea**: Imodium
**Skin Rash**: antibiotics, hydrocortisone cream (please see **Q22** survey findings for additional medications cited to help control treatment induced side effects).

**Q23** identified **40.3%** of patients who were required to pay out-of-pocket expenses to access some of these medications to treat side effects. Expenses ranged from $2.00 to as high as $4500.00. Open-ended replies included:
***"$50/month for creams."*** ***"Annually $1000."***

***"$30-40 every 3 to 4 weeks."*** ***"$325 month for one drug and approx. $40 every 4 months."***
**Q28** and **Q29** highlighted the out-of-pocket expenses paid by patients to access therapies such as immunotherapy (nivolumab + ipilimumab), Xeloda, and Lonsurf + bevacizumab which were considerable. The patient who accessed the immunotherapy incurred a hefty expense of **$150,000.00**, a cost which is quite prohibitive for most Canadians.

Three patients participated in the telephone interviews, allowing CCRAN to capture a significant amount of qualitative data with respect to their treatment journeys. Interviewees provided thoughtful and at times heart wrenching input regarding patients' treatment journeys, describing the drug therapies accessed, the impact on their quality of life and the amount of time to disease progression.

By way of summary, all three patients received a minimum of two previous fluorouracil-based chemotherapy treatment regimens to manage their metastatic disease (FOLFOXIRI/FOLFOX/FOLFIRI), and all of whom also received the anti-VEGF therapy (bevacizumab), as part of their first and/or second line therapy in combination with **FOLFIRI, FOLFOX or 5FU**.

In addition to **FOLFOXIRI**, and **5FU + Bev**, **Patient A** briefly accessed **Lonsurf + Bev** after failing two Phase I clinical trials and then went on to access Fruquintinib. **Patient B** underwent 12 cycles of FOLFOX, a liver resection, 8 cycles of **FOLFIRI + BEV**, 4 cycles of **FOLFOX + Bev**, and an additional 8 cycles of **FOLFIRI + Bev**. After having accessed 12 cycles of **FOLFOX**, **Patient C** accessed Onvansertib with **FOLFIRI + BEV** early on in his treatment journey. All three patients were diagnosed with microsatellite stable (MSS), RAS-mutant disease.

All three interviewed patients are early age onset colorectal cancer patients, diagnosed at **33, 42, and 41 years** of age respectively. At the time of diagnosis, while they were leading productive and happy lives with their families as parents and spouses, they relayed having been "***absolutely devastated and horrified by the news of a stage IV colorectal cancer diagnosis***". Each underwent surgical resection for their primary tumour and systemic therapies began immediately. Each was afflicted with toxic side effects which they describe as debilitating:

**Patient A**: "***With FOLFOXIRI…..I was so sick…I was spending a lot of time in bed. Sicker than a dog. Not knowing if I was gonna throw up. Not able to eat or drink. My husband was letting me sleep. And I suffered from the neuropathy quite badly….I had to stop doing the bev because I was bleeding a lot vaginally and I mean a lot! I eventually had to have ablation. Lonsurf made me throw up a lot. I was constantly throwing up a lot. My cancer has been a *$&*% show. "***

**Patient B** complained about not having any energy on the FOLFOX therapy and couldn't work anymore. Furthermore, when she accessed the FOLFIRI, she found that protocol to be worse in terms of lack of energy and the level of exhaustion which made for a poor quality of life. She found it difficult to ingest food which led her to lose weight and setting in motion a cycle of poor health outcomes. The neuropathy induced by the oxaliplatin was also contributing to a further debilitating state.

**Patient C** describes his lived experience with respect to FOLFOX and FOLFIRI-induced toxicities. Both protocols "knocked" him out "***4 out of the 14 days***". He claims he was "***bad 60-80% of the time for the 4 out of 14 days"***. Some of the side effects he experienced on the chemo regimens were "***nausea, shortness of breath, chemo brain, fatigue was huge,…has permanent neuropathy which happened in the last cycle, diarrhea, constipation, low blood counts"***. He shared that accessing chemo doublets prevented him from taking care of his daughter, nor was he able to work, and it brought on joint pain, which was quite "***bad***". According to **Patient C**, he could not function while undergoing those therapies – he "***was limited, from lifting stuff, and had to take gabapentin***."

Generally, all interviewed patients reported debilitating side effects while undergoing chemotherapeutic treatments for their metastatic colorectal cancer, which compromised their quality of life. While patients may have derived a clinical benefit in terms of response, that response was limited and was accompanied by incapacitating side effects such **as fatigue, nausea, lack of energy, diarrhea, neuropathy, lethargy, and sheer exhaustion** that prevented them from engaging in their own lives in any meaningful way. Diarrhea or nausea/vomiting prevents patients from leaving their homes for they must stay in close proximity to a bathroom. Exhaustion and fatigue confines patients to bed or a couch. Two survey respondents shared (**Q34**):
"***Chemo impacts the system so harshly. The cure can't be worse than the disease***."
"***The need to be able to function every day instead of being so fatigued, it is hard to get out of the bed. The side effects have not changed over the decades!"***
Patients were quite emphatic about their experience with combination chemotherapies which compromised their well being some of or most of the time and necessitated time off work, and led to the inability to care for children, lack of self care, and impacted time spent enjoying life in general. Normal daily activities could not be resumed nor could they spend quality time with their friends and family, robbing them of the freedom to "***live life again***".

Interviewed patients' and surveyed patients' greatest complaint is the inability to bring their disease under control to the point where they can be off treatment for a substantially long period of time such that they are able to experience treatment holidays that are void of cancer-induced symptoms and treatment-induced side effects. In the words of two survey respondents (**Q34**) and (**Q70**):
"***For not curing my cancer or at least NED for a couple years. I was only 1 month NED before recurrence (was) worse than my previous diagnosis***."
"***CRC needs more treatment options, period…… I have been NED 3 times but I cant get rid of the cancer. It keeps coming back in big ways. I need options NOW***."

## Improved Outcomes

Metastatic colorectal cancer patients and their caregivers face significant challenges: the prognosis for these patients continues to be poor and, as such, the goal must be to provide these patients with additional drug therapies that can help to improve, not only longevity, but quality of life. Surveyed patients were asked how important is accessing new effective treatments for colorectal cancer (**Q13**): **95.18%** of respondents believed it to be **very important**. In **Q40** of the survey results, **93.8%** of respondents believe it is very important that when taking a new therapy for their cancer it bring about improvement in their physical condition by way of tumour shrinkage, tumour stability, reduction of pain and improved breathing. Accessing

a new and effective therapy that affords improvements in a patient's quality of life by way of improved mobility, sense of wellness and relief from side effects was "**very important**" to **84.69%** of surveyed patients according to **Q41**.

**95.92%** of patients would take a therapy that could provide better quality of life during their lifetime even if it does not extend survival (**Q43**). And after having been advised there is no other available treatment for their cancer, patients would be prepared to access a toxic therapy, provided an appropriate survival benefit is realized for them; the greater the survival benefit (**2 months, 6 months, 1 year**), the more likely the patient was willing to access a toxic therapy and endure the treatment's toxic side effects (**Qs 44, 45, 46**), according to the following weighted average scores (out of a possible 10): **6.75** (2 months), **6.75** (6 months), and **7.92** (1 year) – though there was no difference between a 2 and 6 month survival benefit. A surveyed patient provided the following open-ended reply:

"***It's important to provide treatment options that allow patients to live a life. No IVs and no bottles. Less time in the hospital***." (**Q59**)

The interviewed patients provided their perspectives on the improvements they would like to see in a new drug therapy, which they believe are currently not available in other previously accessed therapies, notably in the chemotherapies they have accessed (**Q24-26**). They maintain a therapy should regress disease with minimal to no side effects. They prefer a therapy that is designed to cure a patient's cancer. And while the therapy is destroying the cancer, it should not be destroying the balance of the body's healthy tissues, rendering the patient debilitated and unwell. The patient's quality of life should be maintained at all times to ensure they are living their best life **and not a former glimpse of what used to be their life**. If a therapy cannot provide a cure, it should indeed provide a significant extension in survival. A drug therapy should also be conveniently administered: it should be an **orally administered therapy** in the comfort of a patient's home. This would eliminate considerable travel and stress for the patient, their caregiver and the entire family, such that travel costs are avoided and precious time spent away from home is spared – no time should be spent in a chemo suite, enduring painful infusions, allergic reactions and time that could be better spent doing anything but sitting in an infusion chair. Additionally, they emphasized the need for treatments that could provide a durable, longstanding response. **Patient A** shared:

"***I wanna see a therapy that will cure me….We really need a cure, and more oral drugs, cuz patients don't feel good so let's limit imposing upon them by keeping them at home and improving their comfort. And let's get us good quality of life. No more painful, toxic treatments. I am so tired***."

Two of the three interviewed patients (**B and C**) maintained that Fruquintinib possessed the desired improvements, while **Patient A** maintained that it was "***too early to tell if it cures me, then yes. Pill form, then yes, this is an improvement***." According to **Patients B and C**, Fruquintinib is capable of regressing disease, prolonging life while providing improved quality of life, with minimal to no side effects. This is an oral therapy that can permit patients the luxury of resuming daily activities, some of whom were able to resume caring for their young children, and allow them the freedom to appreciate life by spending time with family and friends despite the horrors they endured through toxic treatments. According to **Patient C**:

"***I did. I took trips, I did several things. But it allowed me more time with my daughter who is so young. I got to take her to the park, take her to family vacations together, play with her, that is the greatest gift of all***. ***All because I am not stuck in an infusion chair***."

## Experience With Drug Under Review

Two surveyed patients accessed Fruquintinib therapy as a standard of care (though **Q54** results indicate that it was funded through a pharmaceutical patient support program) and through a clinical trial, both in the third line setting. One patient (**Q53**) commented on Fruquintinib addressing an unmet need: "***the ease of taking a pill instead of going to an infusion centre***". Both patients received fluorouracil-based chemotherapy (with oxaliplatin and/or irinotecan), in combination with bevacizumab, or panitumumab, and finally Lonsurf before accessing Fruquintinib. One patient found Fruquintinib to be less toxic than previously accessed systemic therapies while the other found it to be more toxic relative to previously accessed drug treatments (**Q56**).

Fruquintinib-induced side effects included: abdominal pain, nausea, fatigue, decrease in appetite, and high blood pressure. An additional side effect noted by one of the patients was musculoskeletal pain. The side effects were addressed through the use of pain and anti-nausea medications. **Q59, 61, 63, 66** gauged the two patients' lived experience with the therapy under review: the impact of the treatment-induced side effects on their daily living, the treatment's effectiveness at controlling their cancer, quality of life, and rated Fruquintinib compared to other previously accessed treatments. The first patient would consistently reply with a moderate score of 5/10 and the second patient would consistently respond with an extremely favorable score 10/10.

Both patients agreed, however, that this therapy was much easier to administer and receive than previously administered treatments (**Q62**). Neither patient was required to stop taking the treatment and both believe the therapy should be publicly funded for the treatment of metastatic colorectal cancer in Canada (**Q67**): "***It's another line of therapy that wasn't there before but is there now. Anything that can help the patient potentially live longer is worth trying!***" And, "***We need more options for treatment."***

Our three interviewed patients (**Patients A, B and C**) provided their lived experience with the therapy under review through **Qs12-26** appearing in **APPENDIX 1**. **Patients B and C** accessed Fruquintinib through a clinical trial in the third line setting while **Patient A** accessed the therapy in the fifth line setting through a private payor. Admittedly, these are patients whose tumours harbor a RAS mutation and are, therefore, not candidates for anti-EGFR therapies. They were quite emphatic about ensuring additional therapies come to fruition for this subset of the patient population, as well as, for their MSS disease. This was a point that was well expressed in the survey findings:

"***Not a lot of options when the first 2 run out***." (**Q34**)

**Patient A** is currently a 36 year old female, married with 2 stepchildren who has been experiencing an exceptionally challenging colorectal cancer journey, as evidenced by her input. Her metastatic disease is

confined to her liver, peritoneum, lungs and ovaries and her primary tumour was diagnosed as a distinct subtype of colorectal cancer characterized by the presence of abundant extracellular mucin: mucinous colorectal adenocarcinoma, which she believes has yet to be properly treated with the correct targeted therapies. FOLFOXIRI, two clinical trials and Lonsurf + bevacizumab have not been successful at controlling her cancer. **Patient A** started Fruquintinib therapy in February 2024 and has experienced significant treatment-induced toxicities which she describes as "*crippling her*" due to musculoskeletal pain but is quite grateful to have accessed an oral therapy in the comfort of her own home. In her words: "***No pain, no gain, so perhaps it is working. I believe it is. With the clinical trials, there were no side effects. And it didn't work. With this, I feel like a 100 year old woman, so I really am hopeful!***" She did add that at one point, her abdominal circumference measured 40 cm and is now appearing smaller in size after having accessed Fruquintinib (**Q17**). She rated her QoL while on the Fruquintinib a 4, however, because of the musculoskeletal pain. However, **Patient A** did go on to say: "***It is so easy to use the therapy….that's for sure. I don't have to leave my house. It would be nice if all chemo was like this***." And she went on to say: ***"Fruquintinib has given me another option right now, and I am grateful…that could be saving my life, extending my life…I don't mind enduring the physical hardships, it will give me more of a chance at life, even it it's crippling me right now, it's not the end of the world. I am ok with that. I just want to live.***"

**Patient B** is currently a 42 year old female, married with an 8 year old son. Her metastatic disease is limited to her liver and regional lymph nodes. Having previously accessed FOLFOX, FOLFIRI with bevacizumab, she then accessed Fruquintinib in September 2022 and has received 19 cycles to date (as of the day of the interview). She has experienced hand and foot syndrome, which she states can be challenging at times when walking and at the start of therapy, she did have to start thyroid medication, but today she is "just fine". She shared that she has "***felt fine the entire time, despite the elevated liver enzymes and bout of pancreatitis***." She claims she "***would happily go through it all over again. It is worth it. Because today, I feel fine, and my disease is no longer detectable. It's gone***!"

**Patient B** rated her QoL as a **10!** And added the following:

"…***I can live my life again. I am ok, I am able to work, I am able to work out, and travel, all because of Fruquintinib. I feel great! This is amazing. I am so grateful. That's why I would rate it a 10!***"

She claims the therapy is "***easier to use and she can take the therapy with her regardless of where she goes. She need not go sit in an infusion chair in a hospital….That's the biggest advantage and benefit***."

**Patient C** is currently a 47 year old male, married with a 4 year old daughter. His metastatic disease is located in the his lungs, abdominal lining and retroperitoneal lymph nodes. Having exhausted FOLFOX, FOLFIRI + bevacizumab, and Onvansertib, Fruquintinib was the logical next therapy after having discussed it with his treating oncologist. He accessed the therapy in October 2022 and received 14 months worth. He experienced minor hand and foot syndrome for which he received a lotion to help control it. He also experienced hypertension, joint pain and diarrhea. Medications such as Imodium and Lomotil helped to

control the side effect. He rated his QoL a **9** and according to **Patient C**, he "***does not take that lightly, cuz it was way better than chemo***!" According to the patient, he felt really good and experienced no problems on the therapy. He was never required to stop treatment nor did he have to reduce his dose. He absolutely appreciated the fact that his therapy was orally administered. In his words: "***I was so fine with the pills. I could go out to dinner after taking my pills, that's why I rated it a QoL of 9!***". In January 2024 he went back on FOLFIRI + bevacizumab, and is responding quite well.

**Patients B and C** were elated to have been able to access Fruquintinib. **Patient B** has acquired a No Evidence of Disease (NED) status and **Patient C** believes it has prolonged his life, allowing him to "***recycle a previously accessed therapy",*** thereby, prolonging his life and permitting him more time raising his young daughter. **Patient A** is looking to determine treatment response in an upcoming scan which will justify or invalidate the debilitating side effects.

Accessing the therapy allowed **Patient B** to:

"***start working again as well as working out and moving my body. I do not have to spend hours lying on the sofa recovering from chemotherapy like being tired and having no energy. I like being able to be active and living my life like I used to be able to do. We cancer patients don't usually have that option. But I do now***."

And **Patient C** explains why it was worth accessing Fruquintinib:

"***It stabilized my disease which allowed me more time with my family. Which now allows me the opportunity to access another therapy to which I can respond. It is just giving me more time, more time that is so precious to me because I get to see my little girl grow up***."

None of the three interviewed patients experienced treatment interruptions; **Patient B** who is still on therapy has been prescribed a dose reduction as she achieved a NED status: in her words, "***Had to lower my dose… from 5mg, to 4mg to 3mg***."

In total, 5 patients having the lived experience with Fruquintinib were included in this submission: two from the online survey results and 3 from the qualitative telephone interview data. However, we believe **Patient A** may have contributed to the online survey results. Hence, in total, 4 patients' lived experiences have been captured herein.

While our sample size may be small, the clinical response and improved quality of life being observed is quite remarkable and is irrespective of age, gender, location of primary tumour, treatment line, number of metastatic sites, prior therapy received with bevacizumab, and RAS mutational status or any biomarker status. This clearly indicates, according to the data provided herein (while limited), that Fruquintinib is a viable treatment option for all clinically relevant subgroups of metastatic colorectal cancer.

## Anything Else?

Metastatic colorectal cancer generally cannot be cured through surgical procedures. Hence, treatment principles are primarily aimed at controlling the patient's disease progression and prolonging their survival. As previously mentioned, standard first and second line therapy includes toxic treatments such as 5FU, oxaliplatin, and irinotecan, in combination with an anti-VEGF therapy bevacizumab; and, if RAS wild type, anti-EGFR therapy. After the first two lines of chemotherapy, standard third-line treatment may include Lonsurf + bevacizumab or a less sought after therapy, regorafenib. Once patients progress on these therapies, treatment options include reuse of prior therapies, clinical trials or best supportive care. Consequently, there is an **unmet medical need** for an additional safe and effective treatment. Our patient input underscored this need quite emphatically. Fruquintinib therapy can enhance the treatment landscape in third line and beyond for patients with mCRC, highlighting the importance of sustained inhibition of angiogenesis in the advanced stages. The interviewed and surveyed patients responded well to the therapy under review independent of previous exposure to a VEGF inhibitor. Fruquintinib has the benefit of targeting all three VEGF receptor kinases, making it an ideal and optimal targeted therapy whose activity and success is not reliant on the patient's tumour's biomarker status. Additionally, we feel compelled to include a point related to a clinically relevant subgroup: the **RAS mutated colorectal cancer patient population**. Accessing Fruquintinib in third line and beyond is helping to address **an unmet need** in our refractory colorectal cancer patients whose tumours test positive for one or more RAS mutations and are currently not candidates for targeted therapies. Fruquintinib will provide a new treatment option for these patients with superior quality of life due to fewer and less severe side effects.

Fruquintinib was effective in patients with low and high tumour burden alike and many patients across disease characteristics were able to access and benefit from the therapy. And in patients who were suffering from residual side effects from previously accessed, multiple therapies that had reduced their quality of life, access to Fruquintinib was a pleasant deviation relative to what they had been previously exposed. According to most of the patients with the lived experience, Fruquintinib demonstrated a most manageable toxicity profile, granting them an improved quality of life. They were delighted to have accessed what they described as a highly tolerable therapy, demonstrating a level of benefit unlike any other previously accessed therapy with respect to **quality of life** maintenance. Additionally, to have observed, in some, the magnitude of response in our interviewed patients who had progressed so quickly on prior treatments confirms that Fruquintinib is effective and amenable for long term use. In **Patient B's** final words: "***Of course it's been worth accessing Fruquintinib. So I can continue to live my life to the fullest and be able to do normal activities (spend time with family, work, travel, attend my son's event etc..). I can do all that and feel good at the same time. I couldn't do all that when I was on the chemo. I was too busy feeling exhausted and nauseated.***"

Our surveyed patients provided the following open ended input regarding the funding of Fruquintinib:

"***More options the better."***

***"I want to live longer so having more options available will prolong my life in hopes for a cure."***

***"Options for stage IV patients. There needs to be more options. Limiting these options due to lack of funding is cruel and inhumane. Do better***." And as so eloquently stated by one of our interviewed patients: ***"..it is easy to take, you can continue to live your life with good quality of life, you don't have***

***to sit at an infusion center, you can travel while taking it, I have never felt exhausted while taking Fruquintinib unlike how I felt during chemotherapy, which was horrible….  and I am beyond thankful to have found a drug like Fruquintinib***."

If publicly funded, Fruquintinib would be an extremely important third line and beyond therapy for patients whose disease has been deemed to be refractory or ineligible for current standard of care therapies. Funding this therapy aligns well with the patient perspectives captured within this submission. We, therefore, strongly support and urge that a positive funding recommendation be issued for Fruquintinib for the treatment of metastatic colorectal cancer in third line and beyond. We believe it aligns well with the identified patient need for a new, effective, quickly administered, oral, less toxic treatment option that is capable of maintaining a high quality of life for the metastatic colorectal cancer patient. This should become the new standard of care for this subset of the colorectal cancer patient population.

## Appendix: Colorectal Cancer Resource & Action Network (CCRAN) Conflict of Interest Declaration

To maintain the objectivity and credibility of the CADTH drug 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.

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

NO

**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

**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 |
| Takeda | | | 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: Filomena Servidio-Italiano

Position: President & CEO

Patient Group: Colorectal Cancer Resource & Action Network (CCRAN)

Date: May 21, 202

# Clinician Group Input

## Canadian GI Oncology Network (CGOEN)

CADTH Project Number: **PC0352-000**

Generic Drug Name (Brand Name): fruquintinib (Fruzaqla)

Indication: For the treatment of adult patients with metastatic colorectal cancer (mCRC) who have been previously treated with or are not considered candidates for available therapies, including fluoropyrimidine-, oxaliplatin-, and irinotecan-based chemotherapy, an anti-VEGF therapy, and an anti-EGFR therapy.

Name of Clinician Group: CGOEN – Canadian Gastrointestinal Oncology Evidence Network, and other CRC-treating physicians

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### About the Canadian GI Oncology Network (CGOEN)

The Canadian GI Oncology Evidence Network (CGOEN) is a virtual and inclusive network of Canadian GI Oncology clinicians who contribute to the knowledge of GI cancer and its treatments, including participating in clinical trials, conducting observational research, and involvement in local/provincial and national clinical guideline development and health technology assessment.

## Information Gathering

Information gathered for this submission was based on personal experience in treating patients with metastatic colorectal cancer and expert evidence-based review by Canadian gastrointestinal cancer specialists. Experts contributing to this submission are familiar with the following published information along with data presented at international oncology meetings:

FRESCO and FRESCO 2 – two randomized Phase III trials of Fruquitinib vs. placebo in treatment refractory metastatic colorectal cancer – demonstrating a survival benefit.

Dasari A, Lonardi S, Garcia-Carbonero R, Elez E, Yoshino T, Sobrero A, Yao J, García-Alfonso P, Kocsis J, Cubillo Gracian A, Sartore-Bianchi A, Satoh T, Randrian V, Tomasek J, Chong G, Paulson AS, Masuishi T, Jones J, Csőszi T, Cremolini C, Ghiringhelli F, Shergill A, Hochster HS, Krauss J, Bassam A, Ducreux M, Elme A, Faugeras L, Kasper S, Van Cutsem E, Arnold D, Nanda S, Yang Z, Schelman WR, Kania M, Tabernero J, Eng C; FRESCO-2 Study Investigators. Fruquintinib versus placebo in patients with refractory metastatic colorectal cancer (FRESCO-2): an international, multicentre, randomised, double-blind, phase 3 study. Lancet. 2023 Jul 1;402(10395):41-53. doi: 10.1016/S0140-6736(23)00772-9. Epub 2023 Jun 15. PMID: 37331369

Li J, Qin S, Xu RH, Shen L, Xu J, Bai Y, Yang L, Deng Y, Chen ZD, Zhong H, Pan H, Guo W, Shu Y, Yuan Y, Zhou J, Xu N, Liu T, Ma D, Wu C, Cheng Y, Chen D, Li W, Sun S, Yu Z, Cao P, Chen H, Wang J, Wang S, Wang H, Fan S, Hua Y, Su W. Effect of Fruquintinib vs Placebo on Overall Survival in Patients With Previously Treated Metastatic Colorectal Cancer: The FRESCO Randomized Clinical Trial. JAMA. 2018 Jun 26;319(24):2486-2496. doi: 10.1001/jama.2018.7855. PMID: 29946728

## Current Treatments and Treatment Goals

Treatment of metastatic colorectal cancer is compromised of the use of fluoropyrimidine, irinotecan, oxaliplatin, bevacizumab and anti-EGFR therapy (in KRAS wild type tumors). In a minority of patients - in BRAF mutant tumors – encorafenib with anti-EGFR therapy is available and in dMMR tumors – pembrolizumab is funded. CADTH has provided a positive (clinical) recommendation for trifluridine + tipiracil (Lonsurf) in combination with bevacizumab (Avastin) for treatment-refractory colorectal cancer, with the treatment queued for negotiation with the pan Canadian Pharmaceutical Alliance (pCPA).

Single agent Lonsurf (trifluridine/tipiracil) and Stivarga (regorafenib) are not funded options for patients in Canada. Access is provided via user pay mechanisms. Fruquintinib is currently available via Health Canada's special access program.

Outside of these therapies – local regional options are available for patients for oligometastatic disease such as surgery, ablative techniques or radiotherapy.

The main goal of treatment is the improvement of overall survival and quality of life. With the addition of newer therapies – there has been an increase in the median survival of colorectal cancer to around 2.5 years. The

majority of patients with treatment refractory disease have excellent performance status and remain treatment eligible. This is demonstrated by the rapid accrual of Phase III trials for this population of patients globally.

The ideal treatment in this setting would improve overall survival with manageable toxicity resulting in quality- of-life benefits.

## Treatment Gaps (unmet needs)

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

Currently outside of Quebec – there are no funded treatment options for patients with mCRC who have been treated with Fluoropyrimidine, Irinotecan, Oxaliplatin, Bevacizumab, anti-EGFR monoclonal antibody therapy (if RAS wild type), and encorafenib for patients with the BRAFV600E variant or pembrolizumab for patients with MSI-H. The current option is to consider *user pay* for either trifluridine/tripiracil or Regorafenib, however it is important to recognize that the option of user pay is not accessible for the majority of Canadian patients with CRC, therefore patients will transition to supportive and palliative care.

The majority of patients who have treatment refractory disease have an excellent ECOG performance status and could tolerate further treatment if available that would prolong their survival. Currently the only option is supportive care.

## Place in Therapy

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

Fruquintinib would be considered as per the indication: *For the treatment of adult patients with metastatic colorectal cancer (mCRC) who have been previously treated with or are not considered candidates for available therapies, including fluoropyrimidine-, oxaliplatin-, and irinotecan-based chemotherapy, an anti- VEGF therapy, and an anti-EGFR therapy*.

With the recent recommendation of trifluridine/tripiracil + bevacizumab in the same setting – fruquintinib could be considered in patients who would not be eligible for trifluridine/tripiracil + bevacizumab or in patients post trifluridine/tripiracil + bevacizumab. This would provide patients with two subsequent lines of therapy that were not previously available and resulting in clinically significant improvements in survival.

There will also be patients for whom trifluridine/tipiracil based treatment may not be an option due to myelosuppression concerns, or patients for whom an oral option would be preferable. Thus clinical flexibility is required in this setting.

**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?**

This treatment should be available to patients with metastatic colorectal cancer who have been treated or intolerant of fluoropyrimidine, irinotecan, and oxaliplatin. With respect to biologic and targeted therapies – it should be post encorafenib based therapy in BRAF mutant tumors, post immunotherapy in dMMR tumors,

post anti-EGFR therapies in KRAS wild type tumors and post anti-VEGF therapies. For patients who had not received previous anti-VEGF therapy – they can be considered eligible if their contra-indication has resolved.

Patients would be considered for therapy based on clinician decision and national/international guidelines or consensus statements.

Companion testing is not needed for this drug nor are there subgroups that seem to have a differential response to therapy.

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

While the primary goal is to extend survival (median overall survival is significantly prolonged with fruquintinib) it is also improving current symptoms by shrinking tumour burden and delaying further progression (median progression-free survival was also significantly increased with fruquintinib) and the associated decrease in quality of life and increased symptom burden that comes with that. It is also important to focus on functioning and caregivers. Having an effective treatment to improve symptom burden and delay further deterioration is integral to improving QOL and functioning. This has downstream positive impact on caregivers, and translates to a lower burden of health care use for supportive care.

Patients would be undergoing clinical evaluations on a regular basis for clinical response and toxicity. In addition, routine imaging during timed intervals are performed for objective assessments. Similar outcomes to clinical trials are used to determine benefit to treatment. A meaningful response would be patient preference, tolerability of treatment, quality of life, and response on imaging.

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

Treatment would be discontinued due to disease progression (radiologic or clinical), toxicity, clinician discretion or patient's request.

**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]?**

This treatment could be reasonably to be given in any centre and by any specialist who is currently treating mCRC patients with systemic therapy.

## Appendix: Clinician Group 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.**

**Name: Brandon Meyers**

**Position:** Medical oncologist

**Date:** 13-05-2024

☒ **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 23**

| | Check appropriate dollar range* | | | |
|---|---|---|---|---|
| **Company** | **$0 to $5,000** | **$5,001 to $10,000** | **$10,001 to $50,000** | **In excess of $50,000** |
| AstraZeneca | x | | | |
| Ipsen | | x | | |
| Roche | | x | | |
| Incyte | x | | | |
| Bayer | x | | | |
| | | | | |

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

**Name: Petr Kavan MD**

**Position**: Medical Oncologist Dpt of Oncology McGill University, Co-chair GI oncology Rossy Cancer Network McGill, CRP program director, LDI Jewish General Hospital McGill University

**Date**: 14-May-2024

☒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 2: 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** |
| Merck | | X | | |
| Takeda | X | | | |
| Add or remove rows as required | | | | |

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

**Name: Ravi Ramjeesingh**
**Position:** Medical Oncologist
**Date:** 13-May-2024

☒**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** |
| AstraZeneca | | X | | |
| Amgen | X | | | |
| Roche | X | | | |
| Incyte | | X | | |
| Eisai | | X | | |
| Ipsen | X | | | |
| Merck | X | | | |
| Jannsen | X | | | |

| | | | | |
|---|---|---|---|---|
| Pfizer | X | | | |
| Novartis | X | | | |
| Knight | X | | | |

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

**Name: Jennifer Spratlin**

**Position:** Associate Professor, University of Alberta; Medical Oncologist, Cross Cancer Institute
**Date**: 30-11-2023

☒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 2: 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** |
| Incyte advisor | x | | | |
| Astrazeneca advisor | x | | | |
| Taiho advisor | x | | | |
| Ipsen advisor | x | | | |
| BMS advisor | x | | | |
| Astellas advisor | x | | | |
| BOLD advisor | na | | | |

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

**Name: Vincent Tam**

**Position:** Medical Oncologist, Tom Baker Cancer Centre, University of Calgary

**Date:** 13-05-2024

☒**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** |
| AstraZeneca | | | X | |
| BMS | X | | | |
| Eisai | | X | | |
| Incyte | X | | | |
| Ipsen | | X | | |
| Merck | X | | | |
| Roche | | | X | |

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

**Name: SHARLENE GILL**

**Position:** Medical Oncologist, Professor of Medicine, BC

**Date:** 13-05-2024

☒**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** |
| Takeda | X | | | |
| Taiho | X | | | |

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

**Name: Winson Cheung**

**Position:** Medical Oncologist, Alberta Health Services

**Date:** 14-05-2024

☒**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** |
| N/A | | | | |

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

**Name: Eric Chen**

**Position:** attending physician, Princess Margaret Cancer Center

**Date:**14/05/2024

☒**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** |
| Add or remove rows as required | | | | |

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

**Name: Kevin Zbuk**

**Position:** Associate Professor, Department of Oncology

**Date:** 17-05-2024

☒**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** |
| Add company name | Takeda | | | |
| Add company name | Taiho | | | |
| Add or remove rows as required | | | | |

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

**Name: Benoit Samson**
**Position:** Medical Oncologist
**Date:** 13-05-2024

☒**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** |
| Takeda | X | | | |
| Pfizer | X | | | |
| Jenssen | X | | | |
| Merck | X | | | |
| Amgen | X | | | |

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

**Name: Bruce Colwell**

**Position:** Medical Oncologist, director systemic therapy Nova Scotia Cancer Care Program

**Date:** May 16 2024

☒ **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 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** |
| Jansen | x | | | |
| Merck | x | | | |
| viatris | x | | | |
| Seagen | x | | | |
| Gilead | x | | | |
| Amgen | x | | | |

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

**Name: Rachel Goodwin**
**Position:** Medical Oncology
**Date:** 10-05-2024

☒**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** |
| Pfizer | | | | X,Grant |
| Ipsen | x | X Travel | | X,Grant |
| Apobiologix | | | X,Grant | |
| Bayer | | | | X,QI Grant |
| AAA/Novartis | x | | | |

| | | | | |
|---|---|---|---|---|
| Pfizer | x | | | |
| Amgen | x | | | |
| Mereck | x | | | |
| Astra Zeneca | x | | | |
| Eisai | x | | | |
| BMS | x | | | |
| Roche | x | | | |
| Taiho | x | | | |
| Astellas | x | | | |
| Add or remove rows as required | | | | |

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

**Name: Stephen Welch**

**Position:** Associate Professor, Western University; Staff Medical Oncologist, London Health Sciences Center

**Date:** 11-05-2024

☒**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** |
| Takeda | x | | | |

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

**Name: Jacob Easaw**

**Position:** Professor, Medical Oncology, Cross Cancer Institute, University of Alberta.

**Date:** 13 May 2024

☒**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** |
| Takeda | X | | | |
| Amgen | X | | | |
| Astellas | X | | | |

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

**Name: Hatim Karachiwala**

**Position:** Medical Oncology

**Date:** May 10, 2024

☒**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** |
| Astellas | | X | | |
| Takeda | | X | | |
| Pfizer | | X | | |
| Eisai | | X | | |
| Amgen | | X | | |
| Roche | X | | | |
| Tahio | | X | | |
| Merck | | X | | |
| BMS | | X | | |
| AstraZeneca | | X | | |

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

**1.2 Declaration for Dr. Howard Lim**

**Name: Howard Lim**

**Position:** Medical Oncologist
**Date:** May 21, 2024

☒**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.

| | **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 | | | |
| Bayer | x | | | |
| Amgen | x | | | |
| Takeda | x | | | |
| AstraZeneca | | x | | |
| Astellas | x | | | |
| BMS | | x | | |
| Lilly | x | | | |
| Taiho | x | | | |
| Eisai | | x | | |
| Ipsen | X | | | |
| Roche | X | | | |
| Incyte | | X | | |

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