Fruzaqla™ (fruquintinib) – New drug approval

- On November 8, 2023, Takeda announced the FDA approval of Fruzaqla (fruquintinib), for the treatment of adult patients with metastatic colorectal cancer (mCRC) who have been previously treated with fluoropyrimidine-, oxaliplatin-, and irinotecan-based chemotherapy, an anti- vascular endothelial growth factor (VEGF) therapy, and, if RAS wild-type and medically appropriate, an anti-epidermal growth factor receptor (EGFR) therapy.

- In the U.S, approximately 153,000 new cases of CRC will be diagnosed in 2023, representing 7.8% of all new cancer cases. Approximately 70% of patients with CRC will experience metastatic disease, whether at diagnosis or after treatment.

- Fruzaqla is a kinase inhibitor of VEGFR-1, -2, and -3.

- The efficacy of Fruzaqla was established in FRESCO-2, a randomized, double-blind, placebo-controlled study in 691 patients with mCRC who had disease progression during or after prior treatment with fluoropyrimidine-, oxaliplatin-, irinotecan-based chemotherapy, an anti-VEGF biological therapy, if RAS wild type, an anti-EGFR biological therapy, and trifluridine/tipiracil, regorafenib, or both. Patients were randomized to receive Fruzaqla plus best supportive care (BSC) or placebo plus BSC. The major outcome measure was overall survival (OS), and an additional outcome measure was progression-free survival (PFS).

- The efficacy of Fruzaqla was also established in FRESCO, a randomized, double-blind, placebo-controlled study in China that included 416 patients with mCRC who had disease progression during or after prior treatment with fluoropyrimidine-, oxaliplatin, or irinotecan-based chemotherapy. Patients were randomized to receive Fruzaqla plus BSC or placebo plus BSC. The major outcome measure was OS, and an additional efficacy outcome measure was PFS.

- In both FRESCO-2 and FRESCO, the addition of Fruzaqla to BSC resulted in a statistically significant improvement in OS compared to placebo plus BSC.

	FRESCO-2		FRESCO	
Endpoint	**Fruzaqla + BSC**	**Placebo + BSC**	**Fruzaqla + BSC**	**Placebo + BSC**
OS				
Median, in months (95% CI)	7.4 (6.7, 8.2)	4.8 (4.0, 5.8)	9.3 (8.2, 10.5)	6.6 (5.9, 8.1)
Hazard ratio (95% CI)	0.66 (0.55, 0.80)		0.65 (0.51, 0.83)	
p-value	< 0.001		< 0.001	
PFS				
Median, in months (95% CI)	3.7 (3.5, 3.8)	1.8 (1.8, 1.9)	3.7 (3.7,4.6)	1.8 (1.8, 1.8)
Hazard ratio (95% CI)	0.32 (0.27, 0.39)		0.26 (0.21, 0.34)	
p-value	< 0.001		--	

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- Warnings and precautions for Fruzaqla include hypertension; hemorrhagic events; infections; gastrointestinal perforation; hepatotoxicity; proteinuria; palmar-plantar erythrodysesthesia; posterior reversible encephalopathy syndrome; impaired wound healing; arterial thromboembolic events; allergic reactions to FD&C Yellow No. 5 (tartrazine) and No. 6 (Sunset Yellow FCF); and embryo-fetal toxicity.

- The most common adverse reactions (≥ 20%) with Fruzaqla use were hypertension, palmar-plantar erythrodysesthesia, proteinuria, dysphonia, abdominal pain, diarrhea, and asthenia.

- The recommended dose of Fruzaqla is 5 mg orally once daily for the first 21 days of each 28-day cycle until disease progression or unacceptable toxicity.

- Takeda's launch plans for Fruzaqla are pending. Fruzaqla will be available as a 1 mg and 5 mg capsule.

Optum