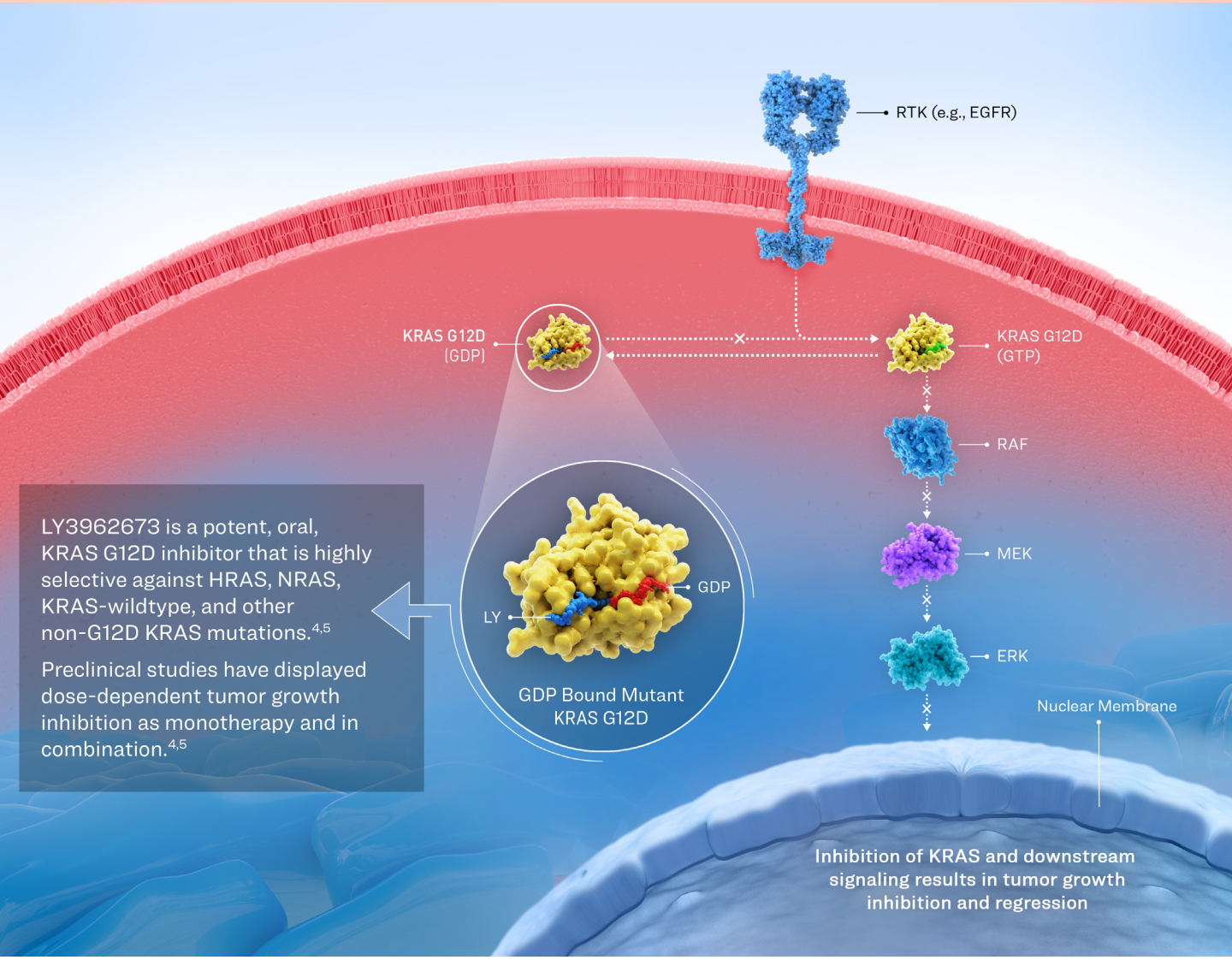
LY3962673

KRAS G12D INHIBITOR

The safety and efficacy of the agents for uses under investigation have not been established. Pipeline molecules may not receive regulatory approval and become commercially available for the uses being investigated. The information provided about new molecules being studied is for scientific information exchange purposes only with no commercial intent. For more information on our pipeline, please visit lillyoncologypipeline.com.

This document was commissioned by Lilly Medical and is intended to be used by HCPs for medical, scientific, and educational purposes.

LY3962673 KRAS G12D INHIBITOR
MECHANISM OF ACTION[1-5]



Kano Y, et al[1], Hofmann MH, et al[2], Ostrem JML, et al[3], Gong X, et al[4], Iyer C, et al[5]

Abbreviations: EGFR=Epidermal Growth Factor Receptor; ERK=Extracellular Signal-Regulated kinases; G12D=Glycine at Position 12 Mutates to Aspartate; GDP=Guanosine Diphosphate; GTP=Guanosine Triphosphate; HRAS=Harvey Rat Sarcoma Virus; KRAS=Kirsten Rat Sarcoma Virus; LY=LY3962673; MEK=Mitogen Activated Protein Kinase; NRAS=Neuroblastoma RAS Viral Oncogene Homolog; RAF=Rapidly Accelerated Fibrosarcoma; RTK=Receptor Tyrosine Kinase.

References: 1. Kano Y, et al. *Nat Commun.* 2019;10(1):224. 2. Hofmann MH, et al. *Cancer Discov.* 2022;12(4):924-937. 3. Ostrem JML, et al. *Nat Rev Drug Discov.* 2016;15(11):771-785. 4. Gong X, et al. Poster presented at: *AACR* 2024. Abstract 3316. 5. Iyer C, et al. Poster presented at: *AACR* 2024. Abstract B115.

The safety and efficacy of the agents for uses under investigation have not been established. Pipeline molecules may not receive regulatory approval and become commercially available for the uses being investigated. The information provided about new molecules being studied is for scientific information exchange purposes only with no commercial intent. For more information on our pipeline, please visit lillyoncologypipeline.com.

This document was commissioned by Lilly Medical and is intended to be used by HCPs for medical, scientific, and educational purposes.

LY3962673 KRAS G12D INHIBITOR

TARGET

KRAS is one of the most frequently mutated oncogenes.[1] Among the various *KRAS* mutations, G12D is the most prevalent, occurring in 37.0% of pancreatic cancer cases, 12.5% of colorectal cancer cases, and 4.9% of non-small cell lung cancer cases.[2] *KRAS* G12D mutations also confer a worse prognosis when compared to *KRAS*-wildtype tumors.[3,4]

MOLECULE

LY3962673 is a selective, oral, non-covalent KRAS G12D inhibitor. Scientists have observed preclinical dose-dependent tumor growth inhibition as monotherapy and in combination with other medicines. LY3962673 is also selective against *HRAS, NRAS,* non-mutated *KRAS,* and other non-G12D-mutant *KRAS*.[5,6]

CLINICAL DEVELOPMENT

LY3962673 is being studied in patients with pancreatic cancer, colorectal cancer, non-small cell lung cancer, or other solid tumors with a *KRAS* G12D mutation.[7]

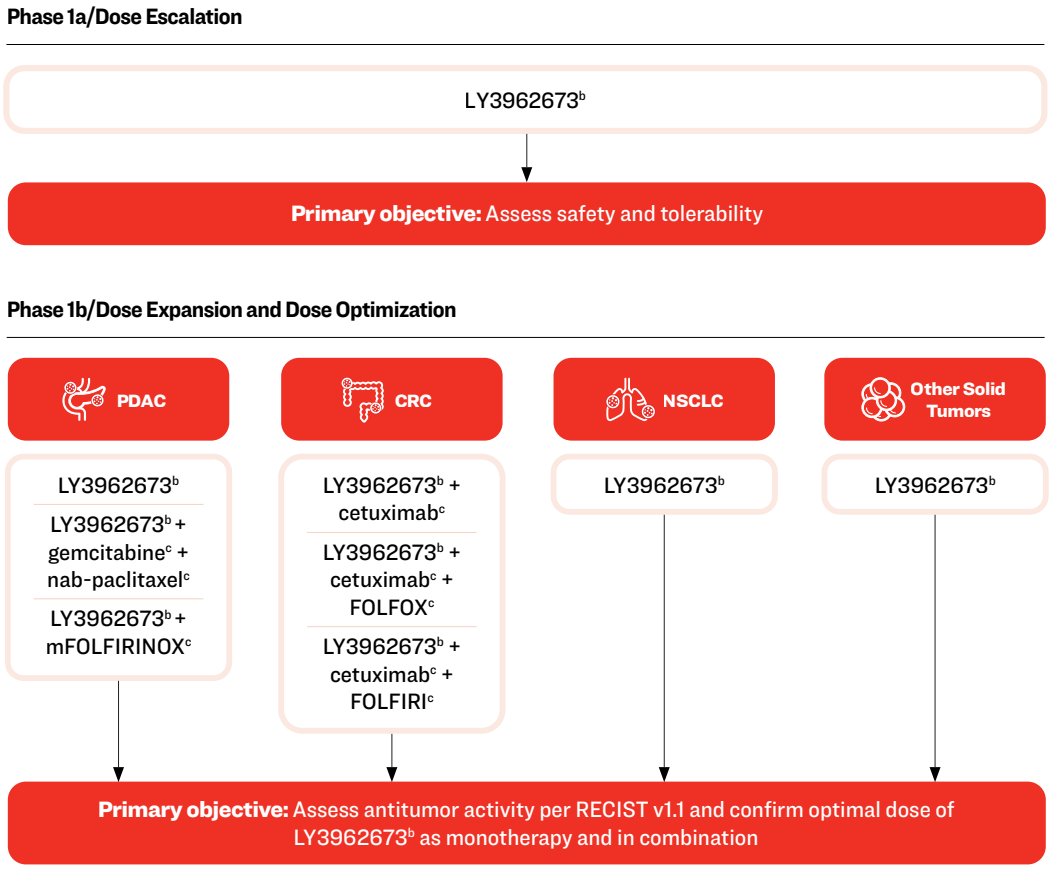
Abbreviations: G12D=Glycine at Position 12 Mutates to Aspartate; *HRAS*=Harvey Rat Sarcoma Virus Gene; *KRAS*=Kirsten Rat Sarcoma Virus Gene; *NRAS*=Neuroblastoma RAS Viral Oncogene Homolog.

References: 1. Kim D, et al. *Nature.* 2023;619:160-166. 2. Hofmann MH, et al. *Cancer Discov.* 2022;12(4):924-937. 3. Bournet B, et al. *Clin Transl Gastroenterol.* 2016;7(3):e157. 4. Ricciuti B, et al. *J Thorac Oncol.* 2022;17(3):399-410. 5. Gong X, et al. Poster presented at: *AACR* 2024. Abstract 3316. 6. Iyer C, et al. Poster presented at: *AACR* 2023. Abstract B115. 7. https://clinicaltrials.gov/study/NCT06586515.

LY3962673 KRAS G12D INHIBITOR

MOONRAY-01

A Phase 1a/1b Trial of LY3962673 in Participants With *KRAS* G12D-Mutant Solid Tumors[a]



[a]This clinical trial is currently being conducted in the USA and Japan. [b]Administered orally. [c]Administered intravenously.

Abbreviations: CRC=Colorectal Cancer; FOLFIRI=Fluorouracil, Leucovorin, and Irinotecan; FOLFIRINOX=Fluorouracil, Leucovorin, Irinotecan, and Oxaliplatin; FOLFOX=Fluorouracil, Leucovorin, and Oxaliplatin; *KRAS*=Kirsten Rat Sarcoma Virus Gene; mFOLFIRINOX=Fluorouracil, Leucovorin, Irinotecan, and Oxaliplatin; NSCLC=Non-small Cell Lung Cancer; PDAC=Pancreatic Ductal Adenocarcinoma; RECIST v1.1=Response Evaluation Criteria in Solid Tumors Version 1.1.

Please visit clinicaltrials.gov for more information on this clinical trial [NCT06586515].

The safety and efficacy of the agents for uses under investigation have not been established. Pipeline molecules may not receive regulatory approval and become commercially available for the uses being investigated. The information provided about new molecules being studied is for scientific information exchange purposes only with no commercial intent. For more information on our pipeline, please visit lillyoncologypipeline.com.

This document was commissioned by Lilly Medical and is intended to be used by HCPs for medical, scientific, and educational purposes.

MOONRAY-01

A Phase 1a/1b Trial of LY3962673 in Participants With *KRAS* G12D-Mutant Solid Tumors (Cont.)

KEY INCLUSION CRITERIA

- Histologically or cytologically proven diagnosis of locally advanced, unresectable, and/or metastatic cancer and measurable disease per RECIST v1.1
- Evidence of *KRAS* G12D mutation in tumor tissue or circulating tumor DNA
- ECOG performance status of ≤1
- Able to swallow tablets
- Select cohorts must have received ≥1 prior line of systemic chemotherapy for advanced or metastatic disease

KEY EXCLUSION CRITERIA

- Known active CNS metastases and/or carcinomatous meningitis
  - Participants with asymptomatic or treated CNS disease may be eligible
- Any unresolved toxicities from prior therapy greater than NCI CTCAE v5.0 Grade 1 at the time of starting trial treatment, except for alopecia, peripheral neuropathy, and ongoing endocrinopathies controlled on appropriate replacement therapy
- Significant cardiovascular disease as unstable angina or acute coronary syndrome, history of myocardial infarction, known reduced left ventricular ejection fraction, or uncontrolled or symptomatic arrhythmias
- Known active hepatitis B, hepatitis C, or untreated HIV
- Active uncontrolled systemic bacterial, viral, fungal, or parasitic infection
- Active malignancy unless in remission with life expectancy of >2 years

Abbreviations: CNS=Central Nervous System; CTCAE v5.0=Common Terminology Criteria for Adverse Events Version 5.0; DNA=Deoxy-ribonucleic Acid; ECOG=Eastern Cooperative Oncology Group; *KRAS*=Kirsten Rat Sarcoma Virus Gene; NCI=National Cancer Institute; RECIST v1.1=Response Evaluation Criteria in Solid Tumors Version 1.1.

Please visit clinicaltrials.gov for more information on this clinical trial [NCT06586515].

The safety and efficacy of the agents for uses under investigation have not been established. Pipeline molecules may not receive regulatory approval and become commercially available for the uses being investigated. The information provided about new molecules being studied is for scientific information exchange purposes only with no commercial intent. For more information on our pipeline, please visit lillyoncologypipeline.com.

This document was commissioned by Lilly Medical and is intended to be used by HCPs for medical, scientific, and educational purposes.

The safety and efficacy of the agents for uses under investigation have not been established. Pipeline molecules may not receive regulatory approval and become commercially available for the uses being investigated. The information provided about new molecules being studied is for scientific information exchange purposes only with no commercial intent. For more information on our pipeline, please visit lillyoncologypipeline.com.

This document was commissioned by Lilly Medical and is intended to be used by HCPs for medical, scientific, and educational purposes.

Pipeline information is current through October 11, 2024.