Silencing Oncogenes at the Level of Gene Expression

Investor Presentation November 2025

Nasdaq: SLXN

Silexion Therapeutics

Forward-Looking Statement

The statements contained in this presentation that are not purely historical are forward-looking statements. Our forward-looking statements include, but are not limited to, statements regarding our or our management team's expectations, hopes, beliefs, intentions or strategies regarding the future. In addition, any statements that refer to projections, forecasts or other characterizations of future events or circumstances, including any underlying assumptions, are forward-looking statements. The words "anticipate," "believe," "continue," "could," "estimate," "expect," "intends," "may," "might," "plan," "possible," "potential," "predict," "project," "should," "would" and similar expressions may identify forward-looking statements, but the absence of these words does not mean that a statement is not forward-looking. Forward-looking statements in this presentation may include, for example, statements about:

- the future performance of the Company, including Silexion's projected timeline for regulatory approvals of its product candidates; and
- the Company's future plans and opportunities.

The forward-looking statements contained in this presentation are based on our current expectations and beliefs concerning future developments and their potential effects on us. There can be no assurance that future developments affecting us will be those that we have anticipated. These forward-looking statements involve a number of risks, uncertainties (some of which are beyond our control) or other assumptions that may cause actual results or performance to be materially different from those expressed or implied by these forward-looking statements. These risks and uncertainties include, but are not limited to, the items in the following list:

- Silexion is a development-stage company and has a limited operating history on which to assess its business;
- Silexion has never generated any revenue from product sales and may never be profitable;
- The approach Silexion is taking to discover and develop novel RNAi therapeutics is unproven for oncology and may never lead to marketable products;
- Silexion does not have experience producing its product candidates at commercial levels, currently has no marketing and sales organization, has an uncertain market receptiveness to its product candidates, and is uncertain as to whether there will be insurance coverage and reimbursement for its potential products;
- Silexion may be unable to attract, develop and/or retain its key personnel or additional employees required for its development and future success;
- Additional factors relating to the business, operations and financial performance of Silexion.

Should one or more of these risks or uncertainties materialize, or should any of our assumptions prove incorrect, actual results may vary in material respects from those projected in these forward-looking statements. We undertake no obligation to update or revise any forward-looking statements, whether as a result of new information, future events or otherwise, except as may be required under applicable securities laws.

Shoot the Messenger

Stop Cancer

Mutated KRAS Proteins Drive Aggressive Cancers

Silexion Develops RNA Silencing Treatments to Abolish KRAS Expression by Silencing Messenger RNA

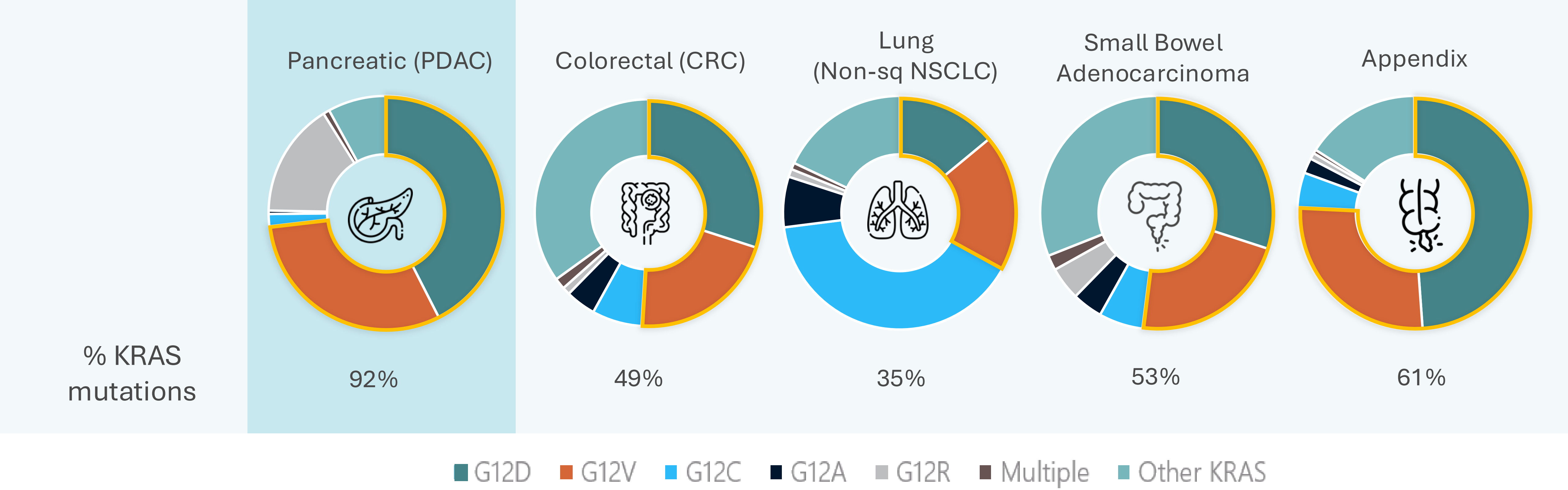
First generation product (Loder) validated in clinical study demonstrating survival benefit

Second generation product (SIL204) designed for enhanced cellular delivery, better stability, and broader antitumor activity

Dual-route treatment administration designed to target both primary tumor and metastases

KRAS is the Prime Target in Multiple Aggressive Cancers

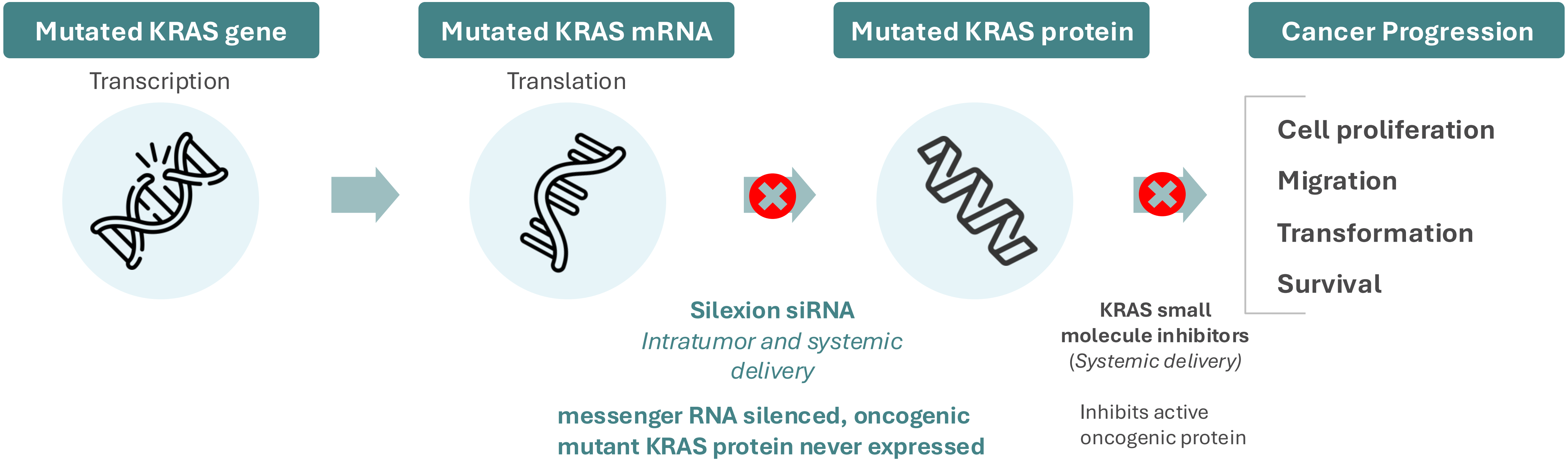
KRAS Mutations Prevalent as Drivers of Various Cancers



CRC=colorectal cancer; LAPC=locally advanced pancreatic cancer; NSCLC=non-small cell lung cancer.
Lee, J.K. et al. NPJ Precis Oncol. 2022;6(1):91.

Silexion's siRNA Platform can Abolish Oncogene Expression

Instead of inhibiting mutated KRAS, Silexion's siRNA platform technology is designed to completely silence oncogene expression, preventing production of mutated KRAS at the outset – potentially superior to existing KRAS inhibitors



Treating closer to the mechanism driving cancer presents a better chance to overcome treatment resistance

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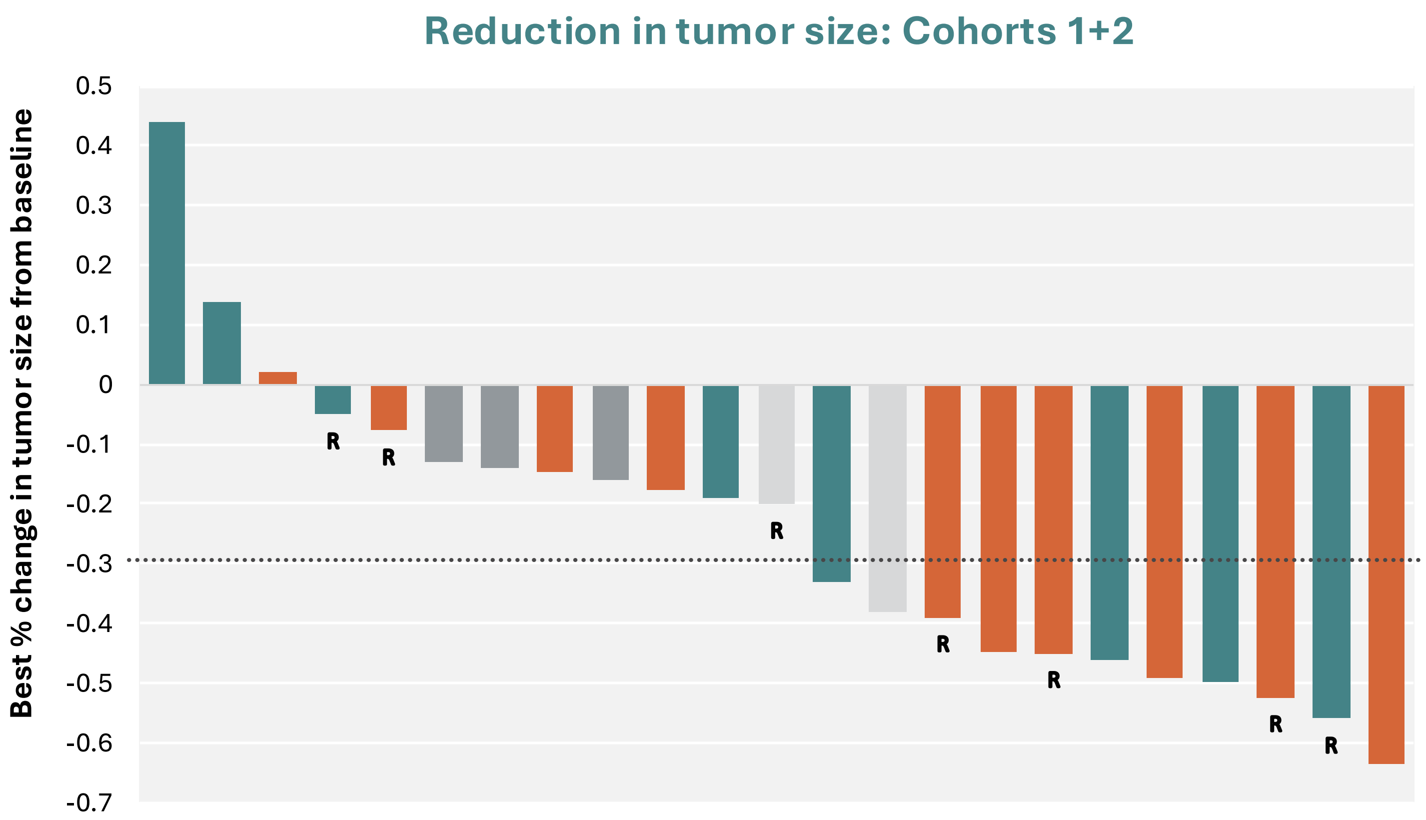
LODER (First generation siRNA)

Phase 2 Clinical Trial Data

First-Generation Mutant KRAS RNA Silencer (Loder) Led to Robust RECIST* Antitumor Activity in mutant KRAS-Driven Locally Advanced Pancreatic Cancer



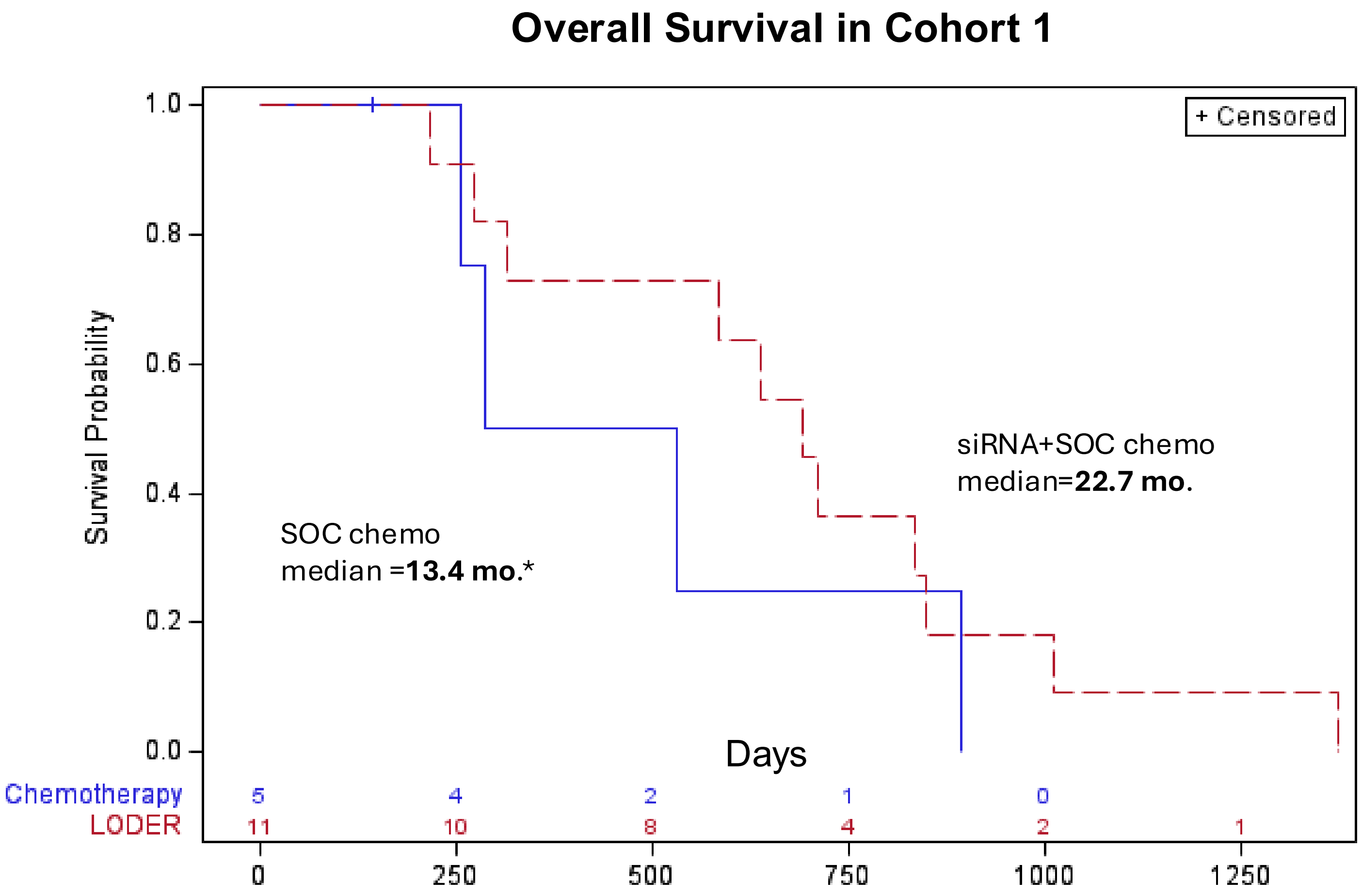
KRAS mutation subtype	G12D	G12V
Chemo		
Loder		

R = Non-resectable tumor becomes resectable

	Cohort 1+2 LODER+Chemo	Chemo
% RECIST* Response	56% (10/18)	20% (1/5)
% RECIST* Response or tumor becomes resectable	67% (12/18)	40% (2/5)

LAPC=locally advanced pancreatic cancer.
*Response Evaluation Criteria in Solid Tumors. Overall response rate was confirmed by RECIST 1.1 of the target tumor, as analyzed by sites.
Bar curves below the solid black line starting at y-axis -0.3 indicates criteria for positive RECIST response.
Cohort 1: non-resectable LAPC, backbone chemo Gemcitabine Plus Nab-paclitaxel
Cohort 2: LAPC or Borderline Resectable Pancreatic Cancer (BRPC), backbone chemo Gemcitabine Plus Nab-paclitaxel, Folfirinox or modified Folfirinox

Cohort 1 LAPC KRAS_G12V or G12D Patients Treated with Loder Had 9.3 Months Improvement in Overall Survival



Hazard ratio (HR)=0.59,
(95% CI, 0.18, 1.96, p=0.39)

Time to death is slower, 41% reduction in the rate of mortality

Patients living longer with Loder+SOC vs. SOC monotherapy

* SoC (Control) OS consistent with recent trials for LAPC (Gemenetzis G, et al. *Ann Surg*. 2019;270(2):340-347).

SIL204 (Second Generation siRNA)

SIL204 has the potential to become the most advanced gene silencing oncology product in clinical development

- Enhanced delivery into cancer cells
- Better stability
- Broader antitumor activity

Optimizations allows for comprehensive approach: intratumor and systemic administrations targeting both primary tumor and metastases

Successful preclinical results in metastatic models demonstrate potential applicability in mutant KRAS+ pancreatic, colorectal and lung cancers

SIL204 Highly Effective with Broad Inhibition Across Human KRAS Mutations at Sub-nanomolar Concentrations

SIL204 maintains and expands the silencing activity of first generation siG12DLoder

Model is a co-transfection setup where human KRAS is transfected in mouse Hepa1-6 cells with Dual-Glo reporter plasmids.

Mutation	Negative siRNA Control	WT KRAS	KRAS G12D	KRAS G12V	KRAS G12C	KRAS G12R	KRAS Q61H*	KRAS G13D*
IC_{50} (nM)		0.16	0.19	0.44	0.47	0.59	0.24	0.37
MAX Inhibition (%)	0-7	91	90	80	73	71	88	88

IC_{50}=half-maximal inhibitory concentration.
*G13D and Q61H tested in separate studies from the G12 mutations and wild type (non-mutated).
Negative siRNA control collected over various studies

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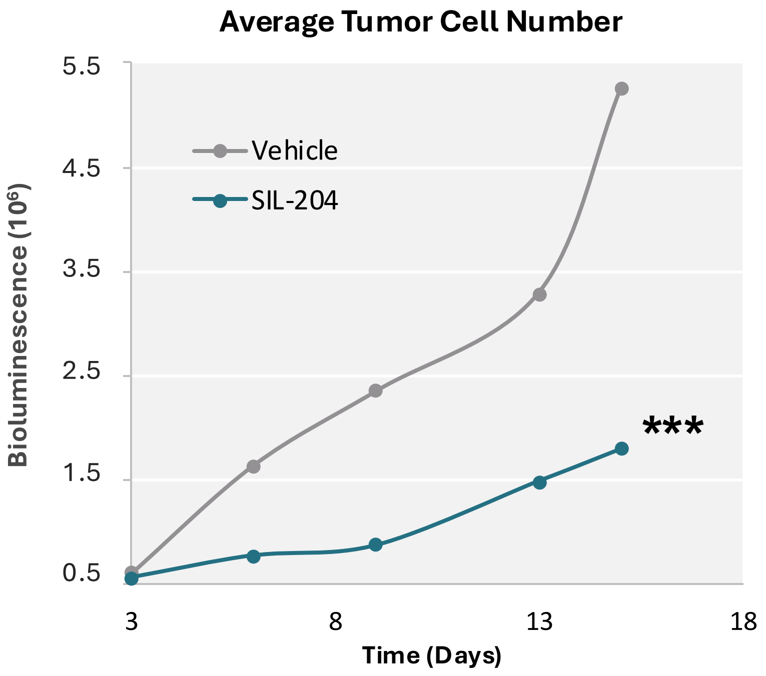
Intratumor Administered SIL204 Inhibited Human Pancreatic Cancer Xenograft Growth in Mice

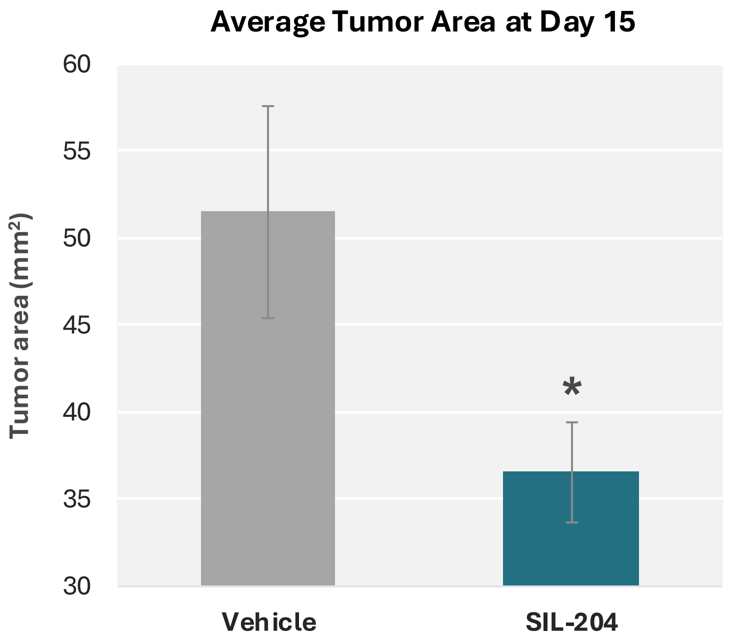
SIL204 significantly reduced tumor volume and growth while increasing tumor necrosis (cell death)

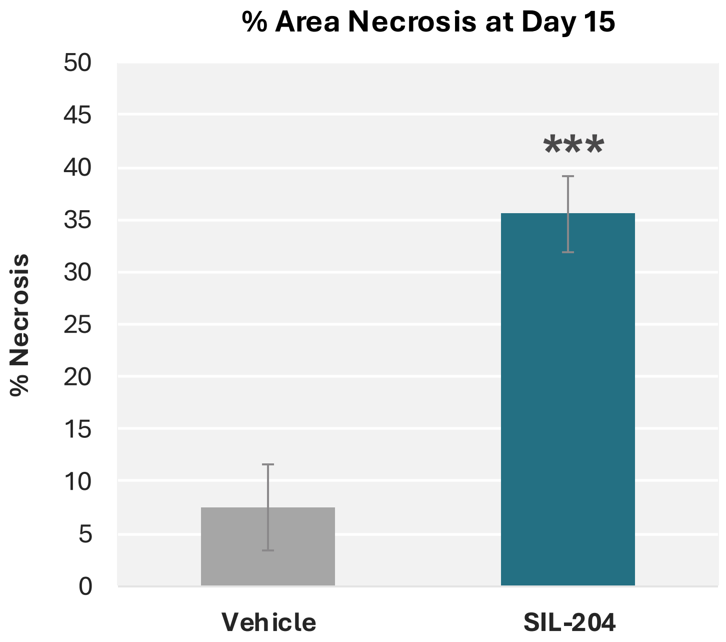
Day 1: Capan-1 (KRAS G12V) luciferase cells were xenografted to mice (s.c.) concurrently with SIL204 formulated in extended-release microparticles

Days 3-15: mice were evaluated for bioluminescence to evaluate relative tumor cell counts

Day 15: tumors were removed, area determined and analyzed by histology for % necrosis from tumor center slice







*p<0.05 ; ***p<0.0005
S.C. = sub cutaneous.

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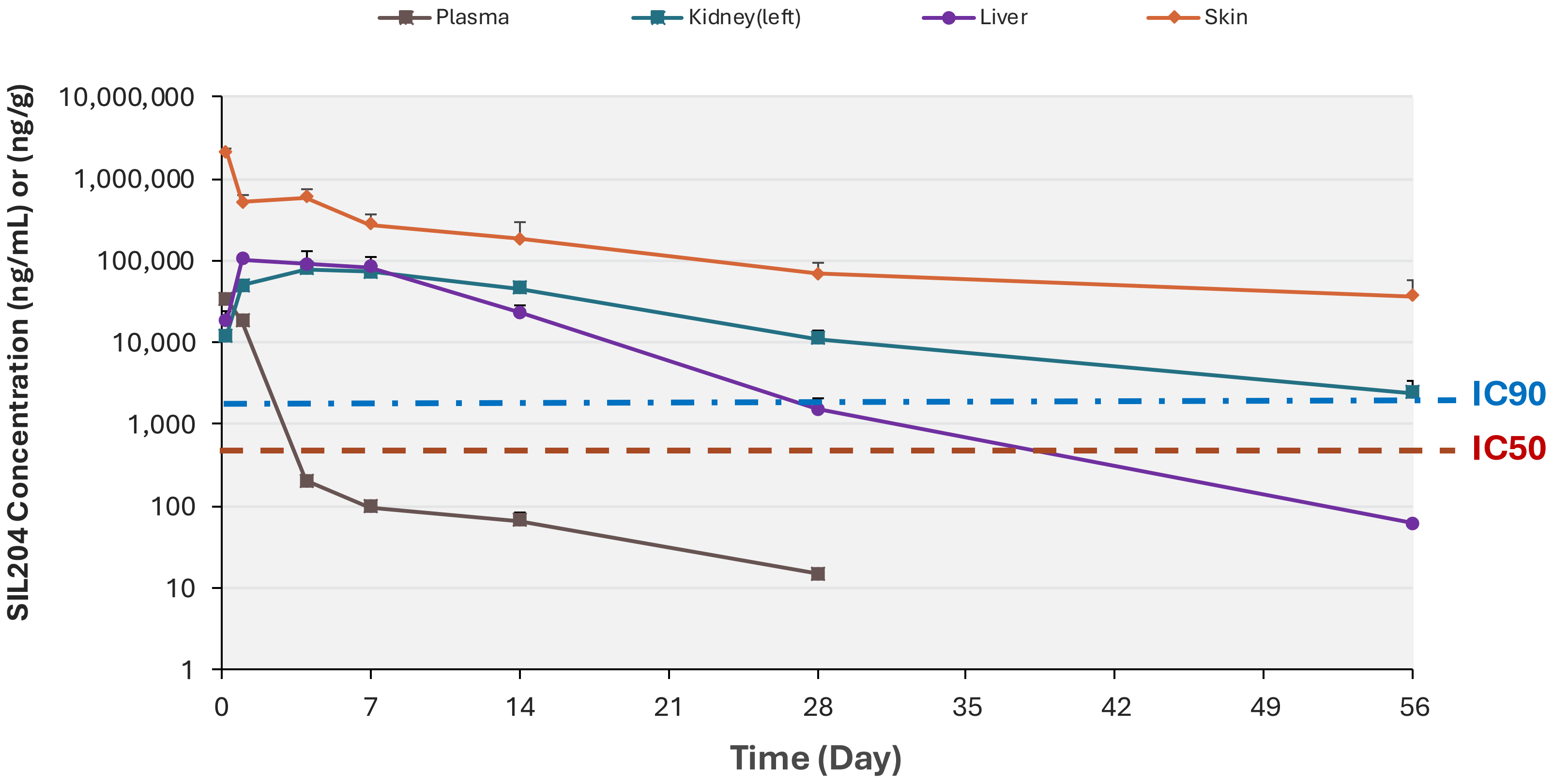
SIL204 Second Generation Enhancements Result in Improved Stability

SIL204 Remains at Substantial Levels for >56 Days in Target Tissues

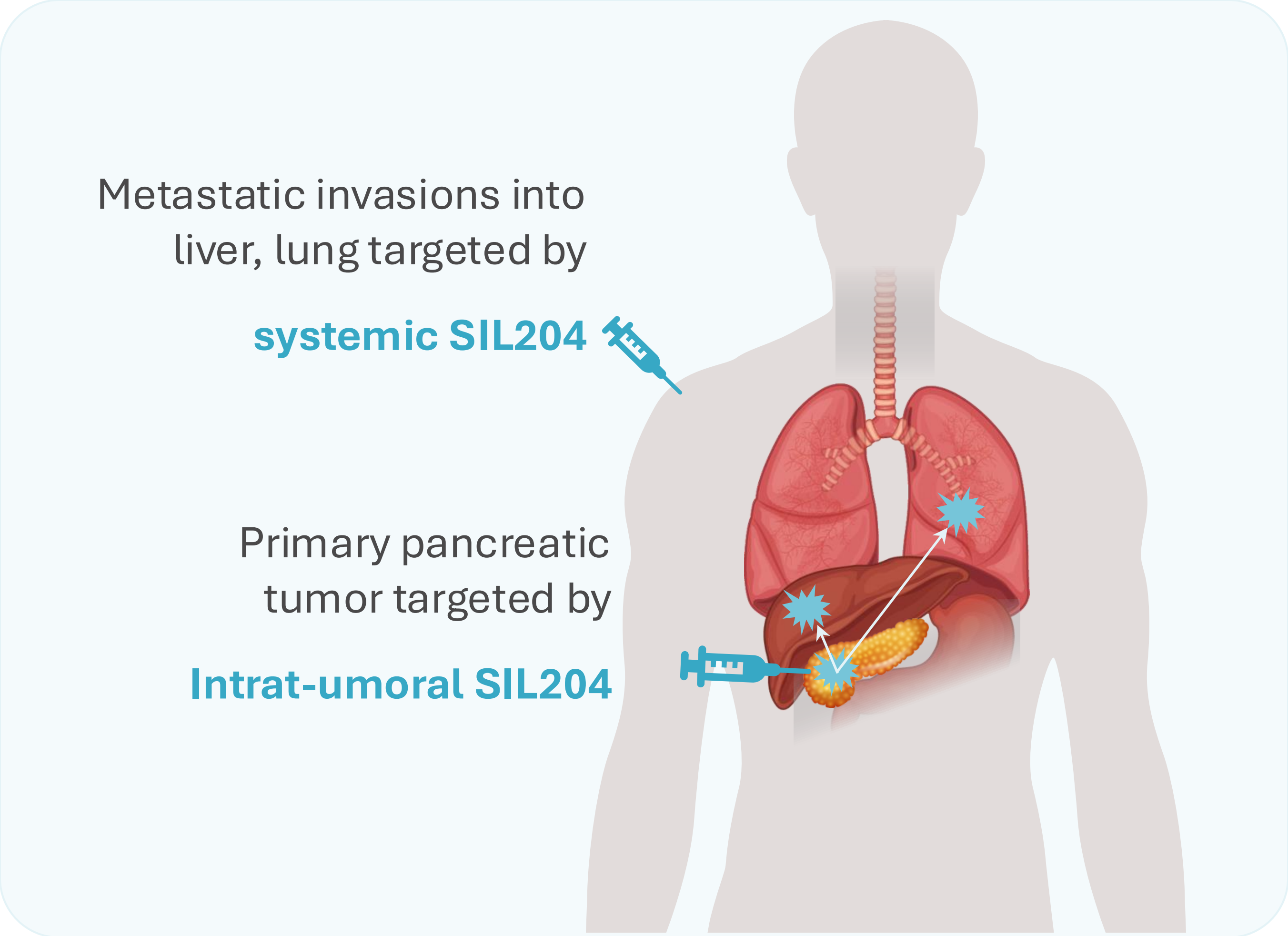


Potential for longer effectiveness of siRNA for treating micrometastases with clinical dosing on monthly basis

 PK profiles of SIL204 after a single s.c. administration were determined in Sprague Dawley rats using a LC-MS/MS analytical method, in the plasma and after collection from kidney, liver, and skin.

Dual Administration of SIL204 Designed to Eradicate Primary Tumor and Metastases

Combining intra-tumoral administration with systemic (subcutaneous) complements the effect of SIL204 on the primary pancreatic tumor with eradication of migrating metastatic cells



Pancreatic cancer lethal due to early and rapid metastases

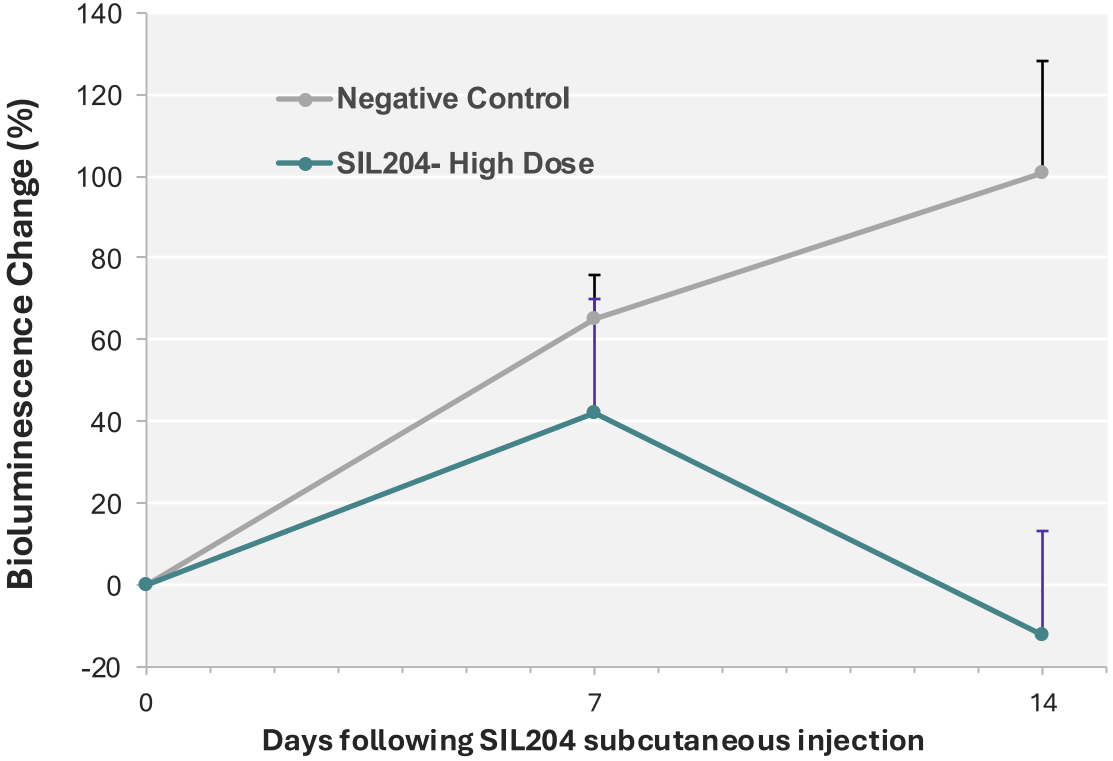
Systemic (SC) administration of SIL204 aims to silence secondary tumors as they are cleared from primary tumor (micrometastases) and those in the pre-metastatic niche before their stromal "barrier" is fully formed

Intratumoral administration of SIL204 aims to silence primary tumor and prevent metastatic "shedding"

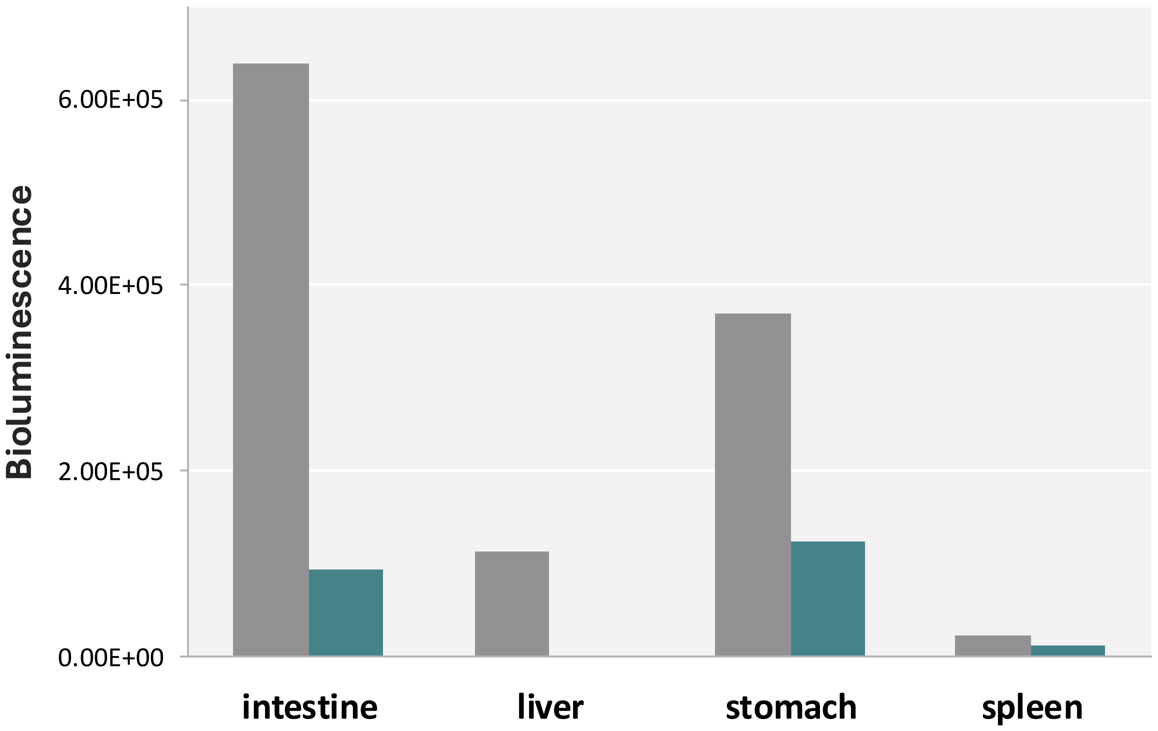
Systemic Administration of siRNA Strongly Supported by Preclinical Data

Subcutaneous SIL204 Proved Effective in Mouse Metastatic Pancreatic Orthotopic Models
Animal model represents human equivalent dose of SIL-204

High dosage subcutaneous injection of SIL204 ablated xenograft tumor



Bioluminescent imaging of metastatic organs



* Human tumor cell line Panc-1 harboring KRAS G12D mutation

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SIL204 Inhibits Growth of Multiple Mutant KRAS+ Human Tumor Cell Lines

Broad Antitumor Activity at Concentrations Achievable with the Planned Clinical Trial Human Equivalent Doses

SIL204 efficacy in tumor cells from 4 different human cancer cell lines: pancreatic; colon; lung and cholangiocarcinoma can be shown in a cell proliferation (CellTiter-Glo (CTG)) assay

Cell line KRAS mutation subtype	IC_{50} (ng/mL)	IC_{90} (nM)	IC_{90} (ng/mL)
A427 (Lung) G12D	**537**	70	1,079
PK59 (Panc) G12D	**1,059**	163	2,496
GP2D (Colon) G12D	**445**	56	852
HS766T (Panc) Q61H	**476**	124	1,907
AVG	**613**	**103**	**1,583**

Results support the pan-KRAS silencing activity observed in transfected hepa cells

IC_{90} is the concentration for 90% inhibition of tumor cell growth, IC_{50} is the concentration to achieve 50% inhibition

SIL204 growth inhibition effect for all tumor lines: IC_{50} = 613 ng/mL, IC_{90} = 1,583 ng/mL

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SIl204 Phase 2/3 Clinical Trial

SIL204 administered intratumorally and systemically as an integrated treatment regimen (IR)
Primary endpoint: Overall survival (OS)
Secondary endpoints: Progression-free survival (PFS), overall response rate (ORR)

Segment 1: Phase 2/3 safety run-in
Initiation Q2 2026
Expected completion Q4 2026

Segment 2: Phase 2 expansion
Initiation Q4 2026

Segment 3: Phase 3 confirmatory
Initiation Q1 2030

2029 Trial Interim results
Sample size adjustment

Segment 1	Segment 2	Segment 3
Design	Design	Design
n=15-18 LAPC subjects treated with SIL204-IR at 3 doses in combination with SoC chemotherapy	Randomized, 3 arms comparing SIL204-IR at 2 doses in combination with SoC chemotherapy vs SoC n=~166	Randomized, 2-arm: SIL204-IR plus SoC chemotherapy vs SoC chemotherapy n=~222
Primary Objective:	Primary Objectives:	Primary Objectives:
Segment 2 doses selection	Segment 3 single dose selection	Efficacy/Safety for marketing approval

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Strategic Collaboration for SIL204 GMP Clinical Supply with Leading European Manufacturers

Collaboration to leverage Catalent and Axolabs' experience in formulation development and manufacturing biologicals to further enhance SIL204's therapeutic potential through improved stability, bioavailability, and delivery precision.

Catalent Limoges Facility

A European Center of Excellence for clinical biologics formulation development and drug manufacture

Axolabs Facility

Leveraging expertise and large-scale nucleic acid production

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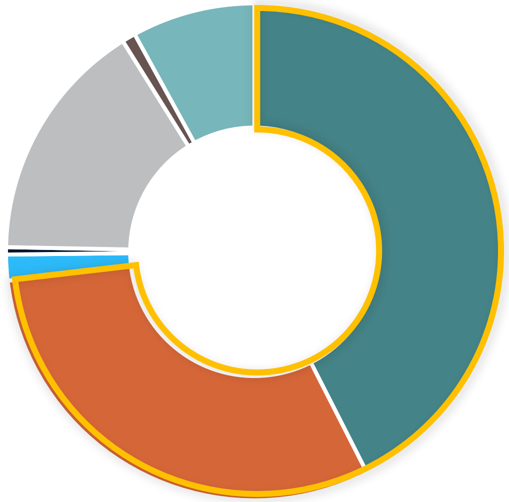
SIL204 Development Strategy in LAPC

2023	2024	H1 2025	H2 2025	H1 2026	H2 2026
	Optimization of siRNA on various fronts; selection of SIL204	Initiate toxicology studies SIL204 GMP production API (SIL204) for First Segment Phase 2/3	GMP production injectable formulation Complete toxicology studies SIL204	Initiate Phase 2/3, LAPC Germany/Israel	
Clinical proof of concept for Loder in LAPC in an approvable endpoint for FDA	Received guidance on trial design from the German Federal Institute for Drugs and Medical Devices (BfArM), intratumor administration	Meeting with German authorities for regulatory buy-in/scientific advice (BfArM) on integrated regimen, and plans to proceed to Phase 2/3 trial	Meeting with Israel Health authorities planned to discuss program	Submit CTA in E.U. for Phase 2/3	• Leverage safety clinical data from first trial segment Phase 2/3 • Pre-IND meeting FDA • Submit IND to FDA • Expand Phase 2/3 to USA\additional EU, etc

SIL204 is the Most Advanced siRNA Formulation for LAPC With a Significant Market Opportunity

KRAS mutations are present in ~92% pancreatic cancer cases[1]

SIL204 targets > 74% of KRAS mutations in PDAC[2] while currently available KRAS G12C treatment are treating ~1.5%



Total Addressable Market in Localized Advanced Pancreatic Cancer

	U.S.	E.U.
Annual pancreatic caner cases	66,400[4]	146,477[3]
KRAS-G12D/V mutated LAPC incidence*	~16,000	~35,000

ROW=rest of the world.
*Number of KRAS G12D/V mutated LAPC were calculated based on KRAS mutations being present in 92% of pancreatic cancer patients, 70-75% with KRAS G12D and G12V mutations and 30-35% of cases being LAPC.
1. Lee, J.K. et al. *NPJ Precis Oncol*. 2022;6(1):91. 2. Yousef, A. et al. *NPJ Precis Oncol*. 20024;8(1):27. 3. Global Cancer Observatory. Pancreatic Cancer. 2022. https://gco.iarc.who.int/media/globocan/factsheets/cancers/13-pancreas-fact-sheet.pdf. 4. National Cancer Institute. Cancer Stat Facts: Pancreatic Cancer. 2023. https://seer.cancer.gov/statfacts/html/pancreas.html.

Strong Intellectual Property Protection

Submissions	Term
Patents supporting siG12DLoder	10 patents issued world-wide, 6 patients pending. Protection until 2030 plus extension
Patents supporting SIL204 • Inhibition of KRAS expression and methods of use thereof include composition of matter	PCT (PCT/ IL2023/051276). Expected protection 2043 plus estimated extension up to 2048) positive patent office review
• Compositions for inhibition of KRAS expression and treatment regiments therewith	Provisional (anticipated up to at least 2046 plus extension)
• siRNA against KRAS G12x for regional perineural invasion or pain associated with a solid tumor	Pending US/EU, expected term till 2040 plus extension

Exclusivity can be extended under country-specific regulatory-based extension rules.

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Thank You

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