Silencing Oncogenes at the Level of Gene Expression

Corporate Presentation September 2024 Nasdaq: SLXN



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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," "project," "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 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.



Company Overview

Clinical-stage company developing proprietary treatments for KRAS-driven cancers

KRAS-Focused RNA Interference Platform with Targeted Delivery	Silexion's siRNA platform technology is designed to silence oncogenes and prevent the production of the mutated KRAS proteins that drive cancer growth
Promising Clinical Data in Locally Advanced Pancreatic Cancer	 Loder siRNA with an extended release PLGA delivery system Completed Phase 2 trial Results observed a 9.3 months improvement in overall survival with Loder + chemo vs. chemo alone Lead candidate SIL-204 optimized upon Loder to enter Phase 2/3 trial
Compelling investment proposition	Nasdaq listed ("SLXN") Late-Stage Ready Asset with Regulatory Path Forward



Focused Pipeline to Address KRAS-driven Solid Tumor Localized Cancers

Program	Indication	Setting	Discovery	Preclinical	Phase 1	Phase 2	Phase 3	Status/ Anticipated Milestone
LODER siG12D + KRAS amplify with extended release PLGA delivery system	Locally advanced pancreatic cancer	Adjunct to chemotherapy	Phase 2 C	ompleted				Phase 2 completed: observed 9.3 month improvement with LODER over SOC. Continue development of SIL-204.
Current Focus: Optimized siRNA	formulation a	nd extended-relea	se delivery					
SIL-204 (Intratumor) KRAS G12D/V + KRAS amplify formulation and extended-release delivery	Locally advanced pancreatic cancer	Adjunct to chemotherapy						H2 2025: CTA submission in E.U. for Phase 2/3 1H 2026: Initiate Phase 2/3
	Colorectal cancer	Adjunct to chemotherapy						H2 2025: Initiate preclinical
SIL-204 (Systemic Adjunct) KRAS G12D/V + KRAS amplify	Locally advanced pancreatic	Adjunct to chemotherapy						Preclinical studies initiated

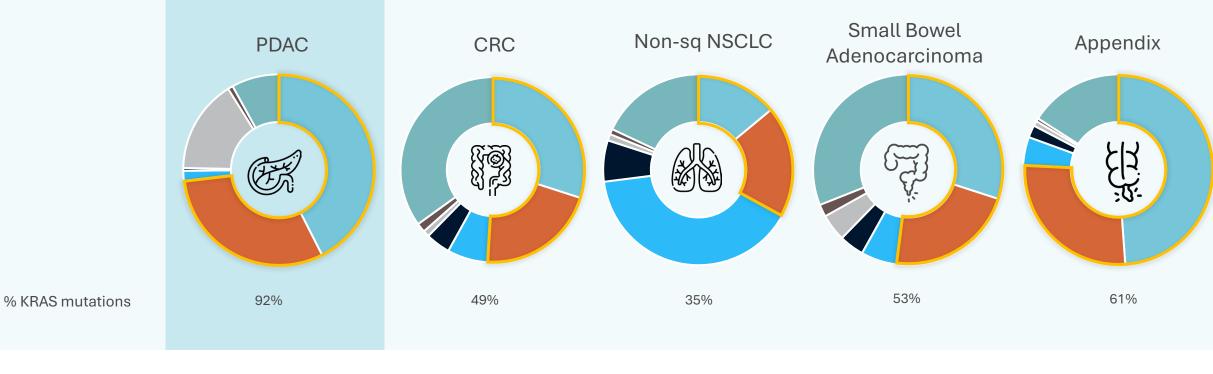


cancer

formulation

KRAS Oncogene is a Validated Target for Numerous Cancers

Prevalence of The Most Common Types of KRAS Mutations Across Cancers



■ G12D ■ G12V ■ G12C ■ G12A ■ G12R ■ Multiple ■ Other KRAS

KRAS is the most common oncogenic gene driver in human cancers with gastrointestinal cancers having high percentages of KRAS G12D/V mutations

CRC=colorectal cancer; LAPC=locally advanced pancreatic cancer; NSCLC=non-small cell lung cancer. 5 Lee, J.K. et al. NPJ Precis Oncol. 2022;6(1):91.



Pancreatic Cancer Has One of the Highest Mortality Rates of All Major Cancers

3rd leading cause today in the U.S.²

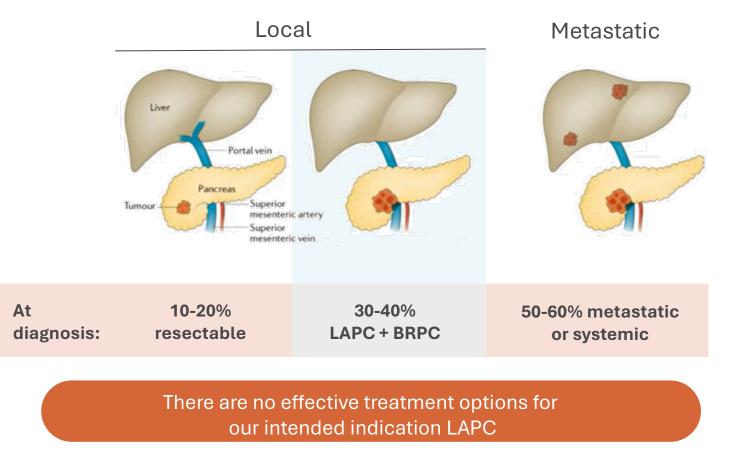
2nd leading cause by 2030²

12.8% 5-year relative survival (2014-2020) is one of the poorest in the U.S.³

Median overall survival for non-resectable PC populations is 14-17 months⁴

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Types and Prevalence of Pancreatic Cancer^{4,5}



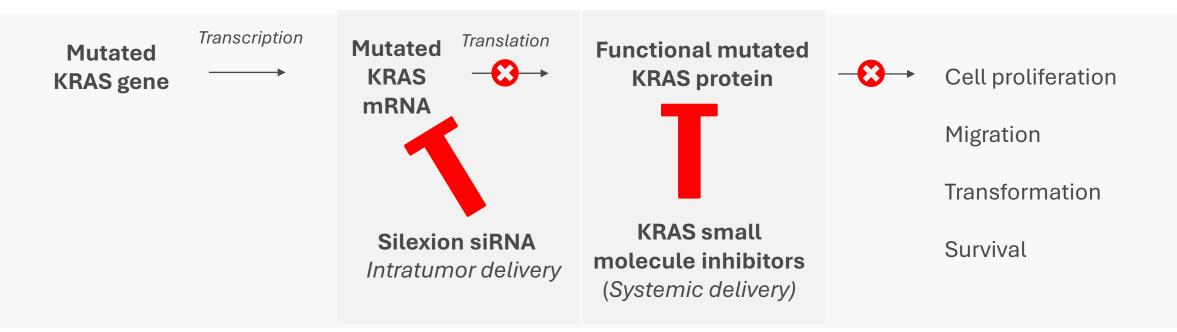
BRPC=borderline resectable pancreatic cancer; LAPC = locally advanced pancreatic cancer.

Bray F, et al. CA Cancer J Clin. 2024;74(3):229-263.
 Hirshberg Foundation for Pancreatic Cancer Research. Pancreatic cancer Facts. https://pancreatic.org/pancreatic-cancer/pancreatic-cancer-facts.
 National Cancer Institute. Cancer Stat Facts: Pancreatic Cancer. https://seer.cancer.gov/statfacts/html/pancreas.html.
 Gemenetzis G, et al. Ann Surg. 2019;270(2):340-347.
 Kleeff J, et al. Nat Rev Dis Primers. 2016;2:16022.



Treating KRAS the Cancer-Driver at the Source and Site of Action

Silexion siRNA technology prevents mutated KRAS from being produced while small molecule inhibitors target the functioning KRAS protein



Silencing oncogene at the production stage is potentially more efficient and safe approach to treat cancer and overcome treatment-resistance



Silexion Innovative **Oncological Approach May** Lead to Significant Improvement in Clinical **Outcomes Over KRAS** Inhibitors

Limitation of currently approved and investigational small molecule KRAS inhibitors:

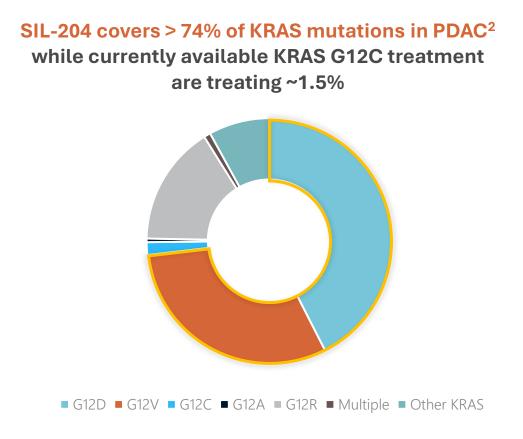
- Treatment resistance
- Requires special monitoring for GI adverse reactions
- Limited overall response rate and progression-free survival
- Low tolerability with adverse events (e.g., rash and GI side effects)

	Silexion's Approach	
Inhibit oncogenic KRAS synthesis before it is active	Intratumor application allows for higher intratumor doses overcoming the tumor's impermeable barrier	Optimized siRNA in the Loder to have enhanced stability, broader activity and new formulation for better delivery

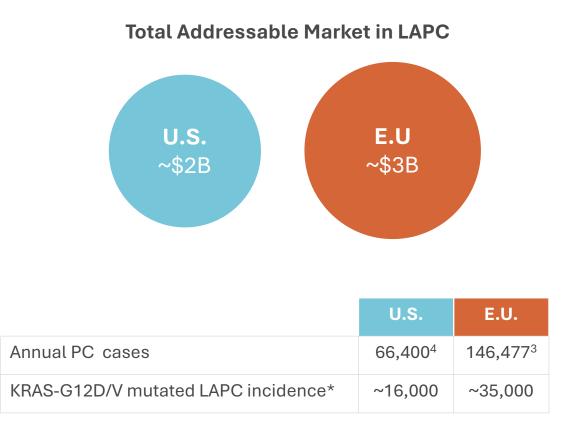


SIL-204 is the Most Advanced siRNA Formulation for LAPC With a Significant Market Opportunity

KRAS mutations are present in ~92% pancreatic cancer cases¹



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LAPC = localized advanced pancreatic cancer; 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.



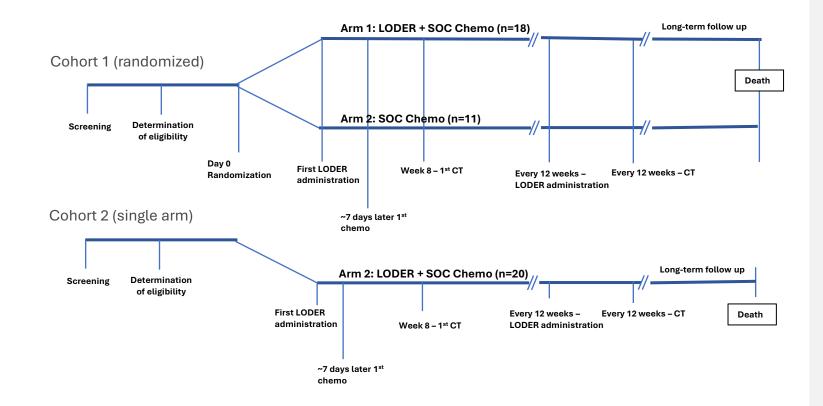
LODER Phase 2 Trial Data





Phase 2 Trial of Loder Completed in 2023 – a Proof-of-Concept

Two-part, open label, study of LODER + SoC chemotherapy vs SoC chemotherapy alone across the U.S. and Israel in patients with non-resectable pancreatic cancer



Key inclusion criteria

Non-resectable without signs of metastasis

ECOG Status ≤ 1

Both cohorts all patients meeting inclusion/exclusion criteria randomized without checking for KRAS mutation status

Endpoints

Overall survival (OS)

Response rate (RR, RECIST v1.1)

Safety

Tolerability



Baseline Characteristics and Cohorts Information

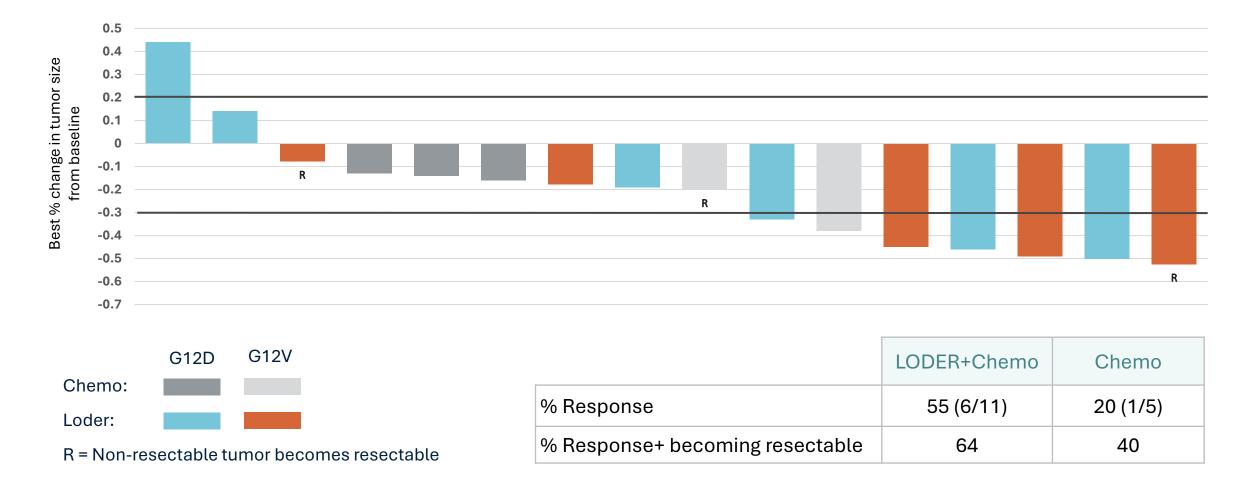
	Cohort 1 (n=29)	Cohort 2 (n=20)			
Design/Arms	Randomized, controlled (SoC)	Single arm			
Population	Locally advanced PC (LAPC)	Non-resectable (BRPC+ LAPC)			
Nationality	62% U.S. (4 sites) , 38% Israel (5 sites)				
Male/ Female %	42% male; 58% female				
Median age (years)	69.7	64.9			
KRAS Mutations	G12D/V*: Loder 11/12, Control 5/10 G12R*: Loder: 1/12, Control 5/10	G12D/V*: Loder 7/9 G12R*: Loder: 2/9			
Avg Loder cycles	2.8	2.1			
Total number of Loder injections	370				
SoC chemotherapy	gemcitabine/nab-paclitaxel (GnP)	(modified) FOLFIRINOX ((m)FFX)			

Due to results of a clinical trial indicating FOLFIRINOX's advantage over GnP as SoC chemotherapy, cohort 2's SoC chemotherapy was changed from GnP (used in cohort 1) to FOLFIRINOX.

*KRAS mutations were determined in 31 patients in total. In cohort 1, 12 patients in the treatment arm and 10 patients in the control arm were tested; in cohort 1, 9 patients were tested. **12** BRPC=borderline resectable pancreatic cancer; GnP=gemcitabine/nab-paclitaxel; LAPC=locally advanced pancreatic cancer; SoC=standard-of-care.



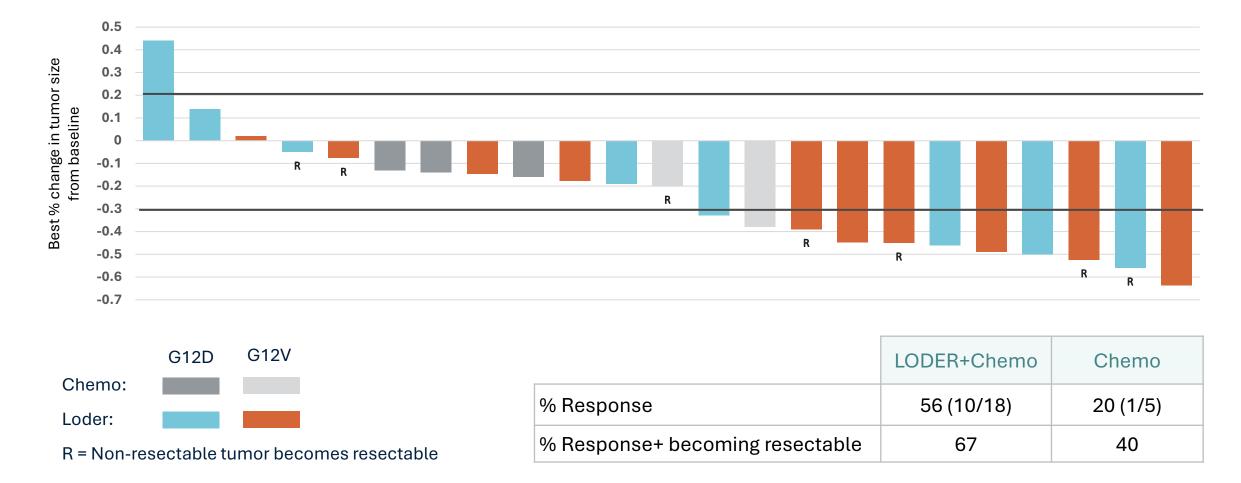
Loder Treatment Led to Robust Objective Response Rate in Cohort 1 Patients with LAPC Harboring G12D/V Mutations*





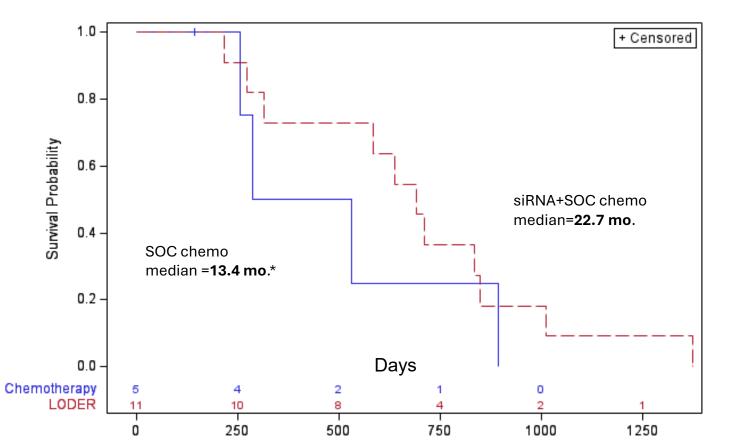


Loder Treatment Led to Robust Objective Response Rate in Cohort 1+2 Patients with LAPC Harboring G12D/V Mutations*





Cohort 1 Patients Treated with Loder Had 9.3 Months Improvement in Overall Survival



OS in Cohort 1

Hazard ratio (HR)=0.59, (95% Cl, 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

7/11 (64%) of patients in LODER+ SoC met RECIST 1.1 criteria vs 1/5 (20%) in SoC chemotherapy



Phase 2 Safety Results

Serious Adverse Events (SAEs) Related to Treatment in Patients with LAPC who Received LODER + Chemotherapy (treatment plus EUS-endoscopy administration procedure)

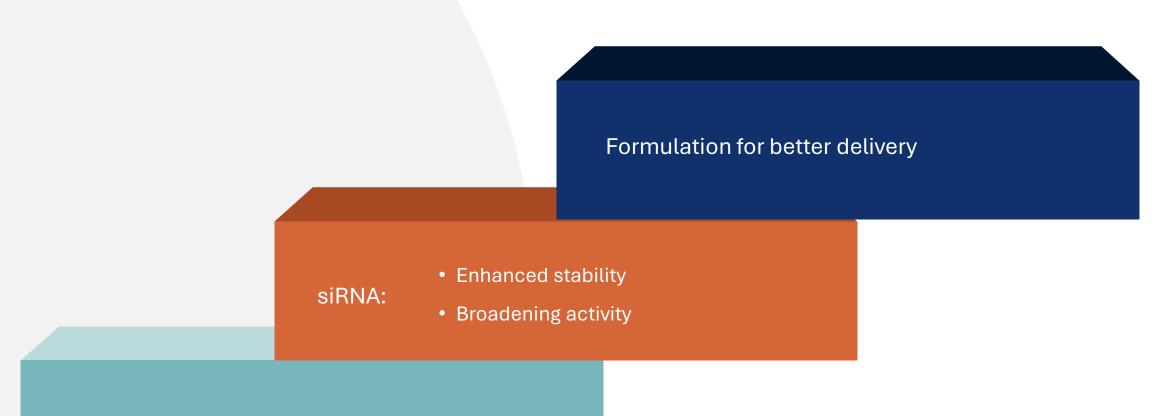
	LODER + SOC chemo (n=38)				
SAE	All grades	Grades 3-4			
JAE	n (%)	n (%)			
Gastrointestinal disorders	3 (8%)	2 (5%)			
Hematemesis	1 (3%)	0 (0%)			
STOMACH ACUTE PAIN	1 (3%)	1 (3%)			
Gastric hemorrhage	1 (3%)	1 (3%)			
General disorders and administration site conditions	2 (5%)	0 (0%)			
Fever	2 (5%)	0 (0%)			
Hepatobiliary disorders	3 (8%)	2 (5%)			
Cholangitis	2 (5%)	1 (3%)			
Obstructive Hyperbilirubinemia	1 (3%)	1 (3%)			
Infections and infestations	2 (5%)	2 (5%)			
Sepsis	1 (3%)	1 (3%)			
Pancreas infection	1 (3%)	1 (3%)			
Depression	1 (3%)	1 (3%)			
Injury, poisoning and procedural complications	1 (3%)	1 (3%)			
procedural hemorrhage	1 (3%)	1 (3%)			
Nervous system disorders	1 (3%)	1 (3%)			
Presyncope	1 (3%)	1 (3%)			



Loder Was Overall Well Tolerated

- The Phase 2 PoC clinical trial investigators reported that Loder treatment was well tolerated; Safety events were primarily related to procedure
 - Intratumor administration of extended-release siRNA via endoscopy (EUS) is safe
- No Treatment Emergent Adverse Events (TEAEs) leading to study discontinuation related to Loder treatment
- No meaningful observations in any vital sign parameter nor any physical examination findings in the study
- Independent Drug Safety Monitoring Board (DSMB) Reviews had no safety concerns nor safety restrictions
- In a subset analysis, no measurable amount of Loder was detected (<BLQ) in any plasma samples suggesting low systemic levels





Building upon the Loder results, we optimized:



SIL-204

KRAS G12D/V and KRAS amplification siRNA formulation





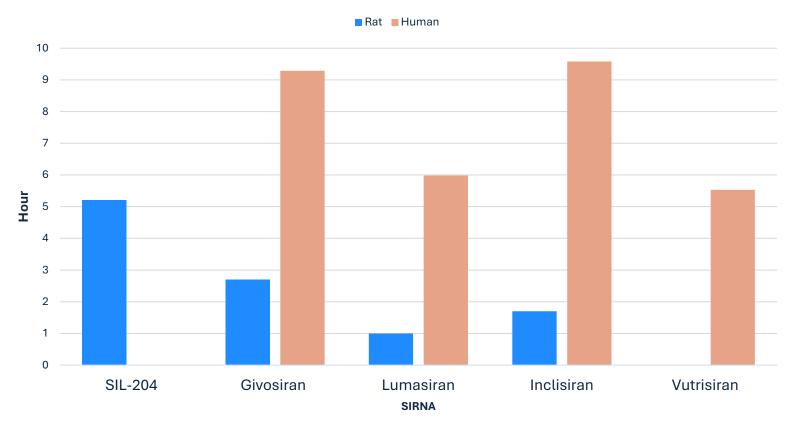
Leveraging Loder Clinical Data to Further Improve SIL-204 Potential Efficacy and Safety

	LODER	SIL-204
siRNA target	KRAS G12D/V+ KRAS amplify	KRAS G12D/V+ KRAS amplify, potential pan KRAS
Stability in human serum	<1 hr	> 48 hrs
Access to tumor cell site of action	No hydrophobic lead	Added hydrophobic lead to increase siRNA access into cell
Extended-release profile	PLGA depot rods	PLGA microparticles suspension for better continuous 3-month release
Route and Ease of administration	EUS-endoscopy* with larger needle; Required loading device	EUS Endoscopy* with smaller and more flexible needle; No loading device needed
Improvement in OS with chemo vs. chemo alone	+ 9.3 months	TBD in Phase 2/3 trial with expected improvement in OS
Safety	Generally well tolerated; Safety events were primarily related to procedure	Expectations for similar safety profile



SIL-204 is Stable In Vivo in Rats for Five Hours

siRNA Half-Life in Rats and Human Plasma (not a head-to-head comparison)



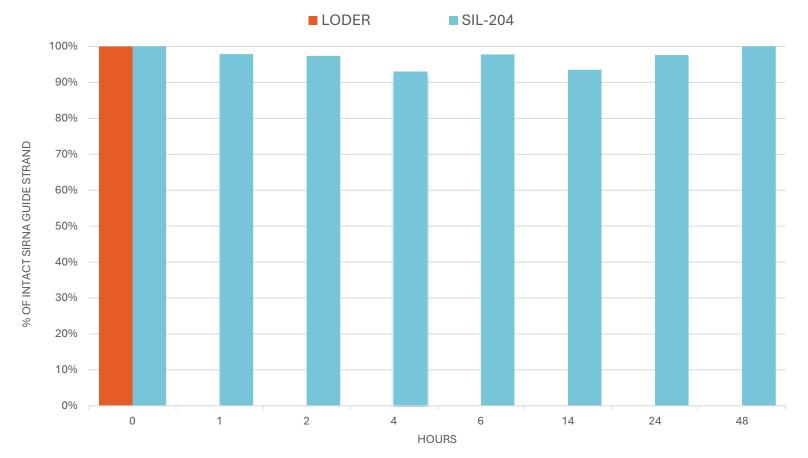
siRNA half-life in humans is 4-6x higher than in rats¹⁻⁸ potentially suggesting SIL-204 may be the most stable siRNA

1. Givlaari (givorisan). EMA. 2. Alnylam. Givosiran NDA MULTI-D.SCIPLINE REVIEW. 3. Lumasiran. Review (fda.gov). 4. Lumasiran. Leqvio, INN-inclisiran (europa.eu) . 5. Inclisiran. Leqvio, INN-inclisiran (europa.eu) . 6. Inclisiran EMA Assessment Report. 7. Vutrisiran. FDA Review Summary. 8. EMA/FDA Approved siRNA Drugs: ADME Study Overview and Data Interpretation.



SIL-204 is Stable In Vitro for Over 48 Hours in Human Serum

siRNA strand placed in human serum and tested for stability



Stability of siRNA Strand in Human Serum

Potentially longer effectiveness of siRNA

Greater ability to diffuse throughout the fibrous tumor environment

Potential in other indications

Silexion

Previous studies have shown siG12D (Loder) half-life to be 5 min in human serum.

SIL-204 Robustly Inhibited the Various Human KRAS Mutations at Sub-nM Conc.

SIL-204 maintains and expands the silencing activity of the Loder

	Maximum Silencing (%) of KRAS G12x Mutations / IC ₅₀ (nM)					
	Non-mutated	G12D	G12V	G12C	G12R	G13D*
External ID						
	91	90	80	73	70	88
SIL-204	0.16	0.19	0.44	0.47	0.59	0.37
siG12D-						
(Loder)**	93	96	71	35	69	

Model is a co-transfection setup in mouse Hepa1-6 cells with Dual-Glo reporter plasmids

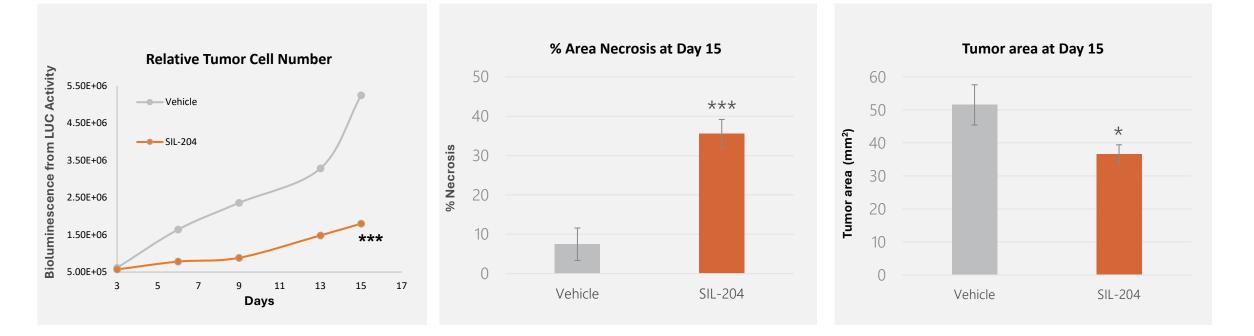
- * G13D tested in separate study from the G12 mutations and wild type (non-mutated)
- ** Loder completed Phase 2 clinical trial



SIL-204 Inhibited Human Pancreatic Cancer Xenograft Growth in Mice

SIL-204 significantly reduced tumor volume and growth while increasing the necrosis (cell death) within the tumor

Day 1: Capan-1 (G12V) luciferase cells were xenografted to mice (s.c.) concurrently with SIL-204 formulated in an extended-release system **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



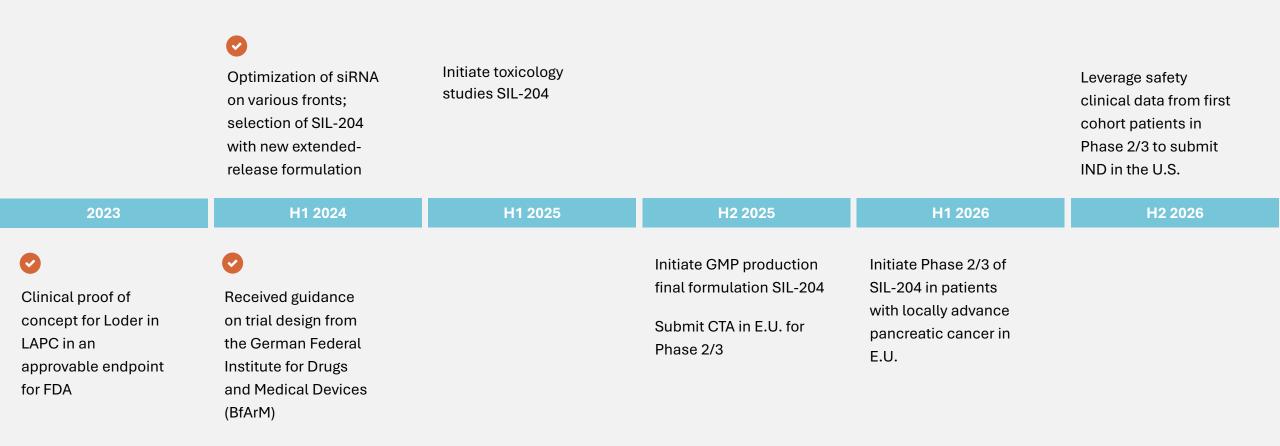
* p<0.05; ** p<0.005; ***p<0.0005

S.C. = sub cutaneous

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SIL-204 Development Strategy in LAPC



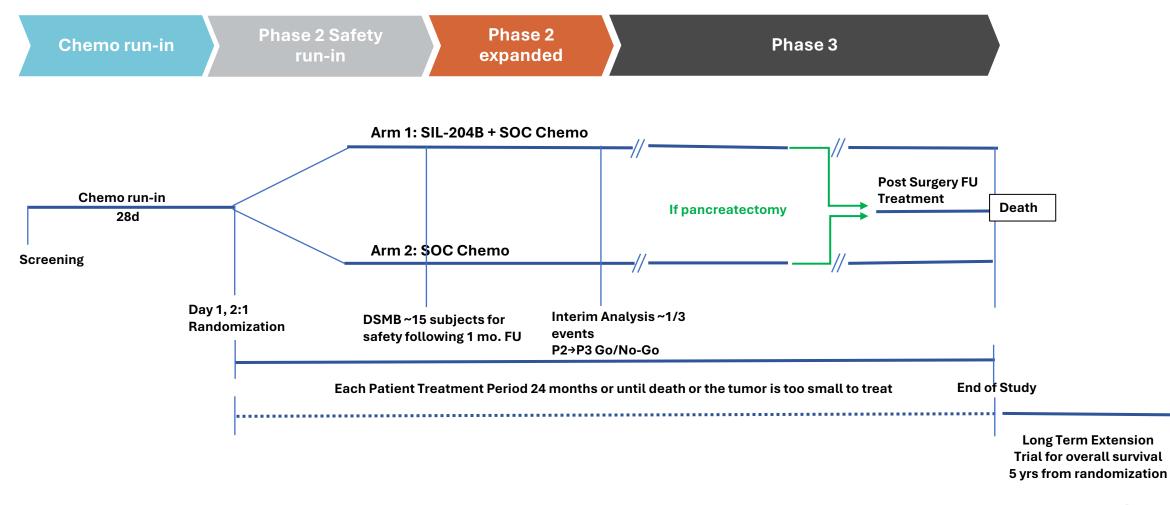
Indicates completed activity. Unmarked activities to be performed.



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Phase 2/3 Trial of SIL-204 in LAPC: Study Design

Received positive guidance from German regulatory agency on suggested trial design.





World-Renowned Expert Scientific Advisory Board



Eileen M. O'Reilly, MD

Memorial Sloan Kettering, NY, NY

Winthrop Rockefeller Endowed Chair of Medical Oncology; Co-Director, Medical Initiatives, David M. Rubenstein Center for Pancreatic Cancer Research; Section Head, Hepatopancreatobi



Milind Javle, MD

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Talia Golan. MD Sheba Tel Hashomer Hospital,, Israel Head, Sheba Pancreatic Cancer Center - SPCC



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Highly Experienced Leadership Team



Ilan Hadar, MBA Chairman and Chief Executive Officer

> 25 years of multinational managerial and corporate experience with pharmaceutical and high-tech companies



Mitchell Shirvan, PhD, MBA Chief Scientific and Development Officer > 25 years of experience in R&D, innovation and discovery in biotech companies

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Mirit Horenshtein Hadar, CPA Chief Financial Officer

> 15 years of corporate finance experience in senior financial positions of public companies and privately held companies, in the pharmaceutical and high-tech industries





Ilan Levin, Director

Former Chairman & Chief Executive Officer of Moringa Acquisition Corp with 25 years of experience as an executive and venture capital/private equity investor in high-tech, Israel-related ventures





Pfizer



Investment Highlights

Advanced RNA therapeutic candidate in oncology

Late-Stage Ready Asset with Regulatory Path Forward

Strong Partnerships with Solid IP Portfolio

- Clinical-stage company with proprietary oncogene siRNA platform
- Intratumor siRNA delivery for pancreatic cancer allow for better drug exposure compared with systemic KRAS inhibitors
- Phase 2 clinical trial with Loder in LAPC showed 9.3 months improvement in the FDA approvable endpoint of overall survival
- Lead Candidate SIL-204 with enhanced siRNA stability, and a better extended-release profile
- Guidance received from German Federal Institute for Drugs and Medical Devices (BfArM) on Phase 2/3 trial
- Submit CTA in E.U. in H2 2025 and initiate Phase 2/3 trial of SIL-204 in 1H 2026
- Plan for U.S. IND submission with clinical safety data from limited number of patients the trial in E.U.

- Established partnerships for GMP production of siRNA and delivery system
- Strong IP portfolio for siRNA and microparticles with exclusivity through December 2043 with extension



Thank You

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