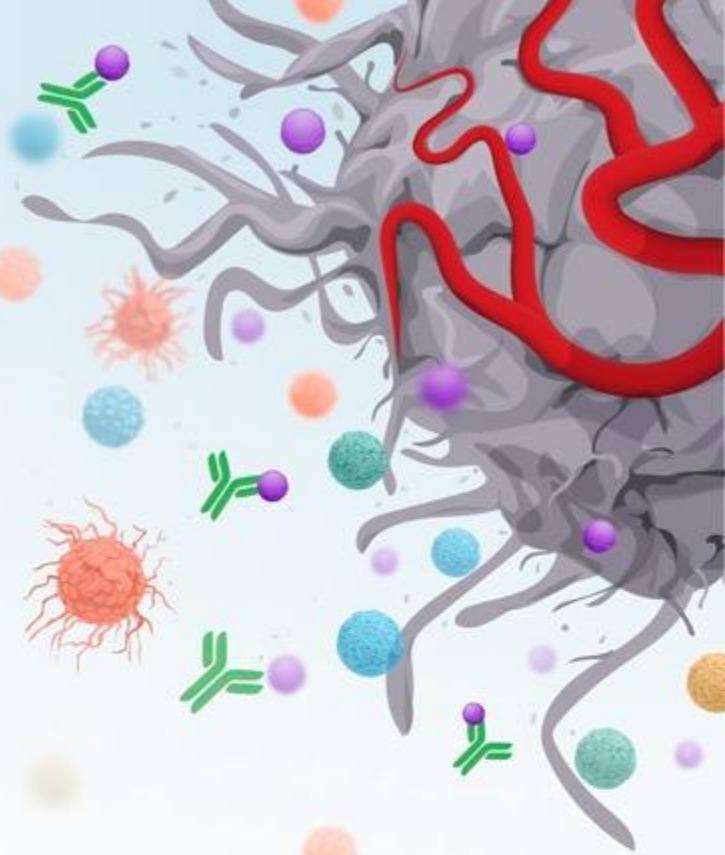
LEAP THERAPEUTICS

company presentation

J.P. Morgan 43rd Annual Healthcare Conference
January 15, 2025



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Forward looking statements

This presentation contains forward-looking statements that involve substantial risks and uncertainties. All statements, other than statements of historical facts, contained in this presentation, including statements regarding our strategy, future operations, clinical trials, collaborations and partnerships, future financial position, future revenues, projected costs, prospects, plans and objectives of management, are forward-looking statements within the meaning of U.S. securities laws. The words “anticipate,” “believe,” “estimate,” “expect,” “intend,” “may,” “plan,” “predict,” “project,” “target,” “potential,” “will,” “would,” “could,” “should,” “continue,” and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words.

Forward-looking statements are neither historical facts nor assurances of future performance. Instead, they are based only on our current beliefs, expectations and assumptions regarding the future of our business, future plans and strategies, projections, anticipated events and trends, the economy and other future conditions.

Because forward-looking statements relate to the future, they are subject to inherent uncertainties, risks and changes in circumstances that are difficult to predict and many of which are outside of our control. We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. These and other risk factors are listed from time to time in reports filed with the Securities and Exchange Commission, including, but not limited to, our Annual Reports on Form 10-K and our Quarterly Reports on Form 10-Q. We assume no obligation to update any forward-looking statements, except as required by applicable law.

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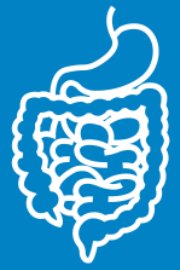
Developing biomarker-targeted antibody therapies for cancer patients

Lead clinical stage antibody program – sirexatamab (DKN-01) targeting DKK1

Multiple upcoming milestones from two randomized clinical trials



Biomarker strategy, focus on GI cancers

Cash runway to Q2 2026 with $62.8M cash at September 30, 2024

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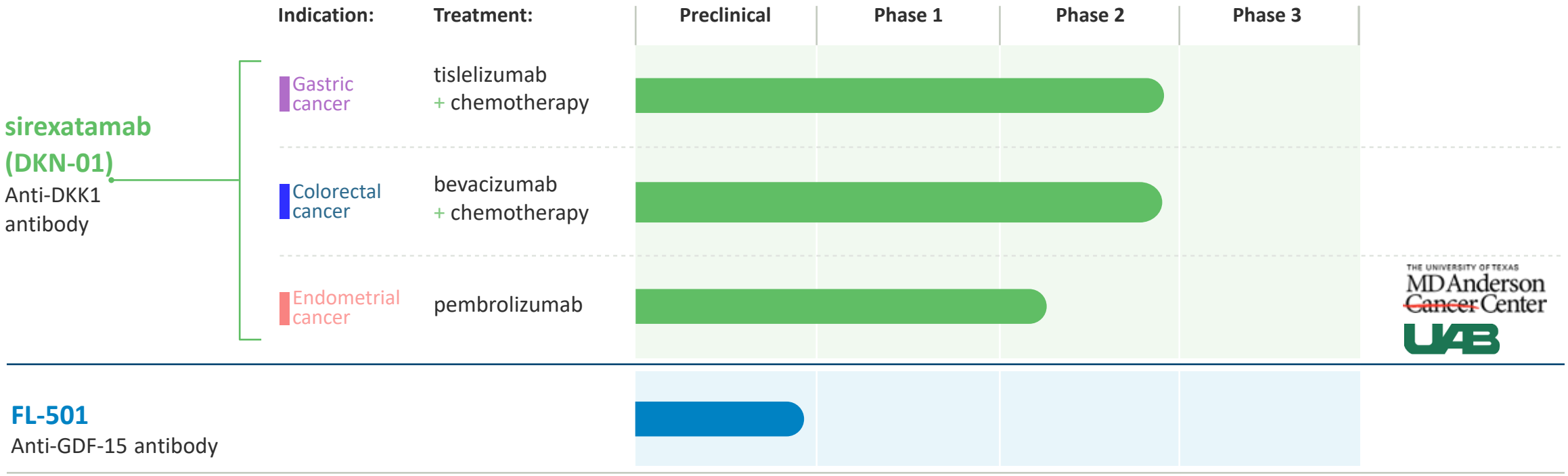
Pipeline



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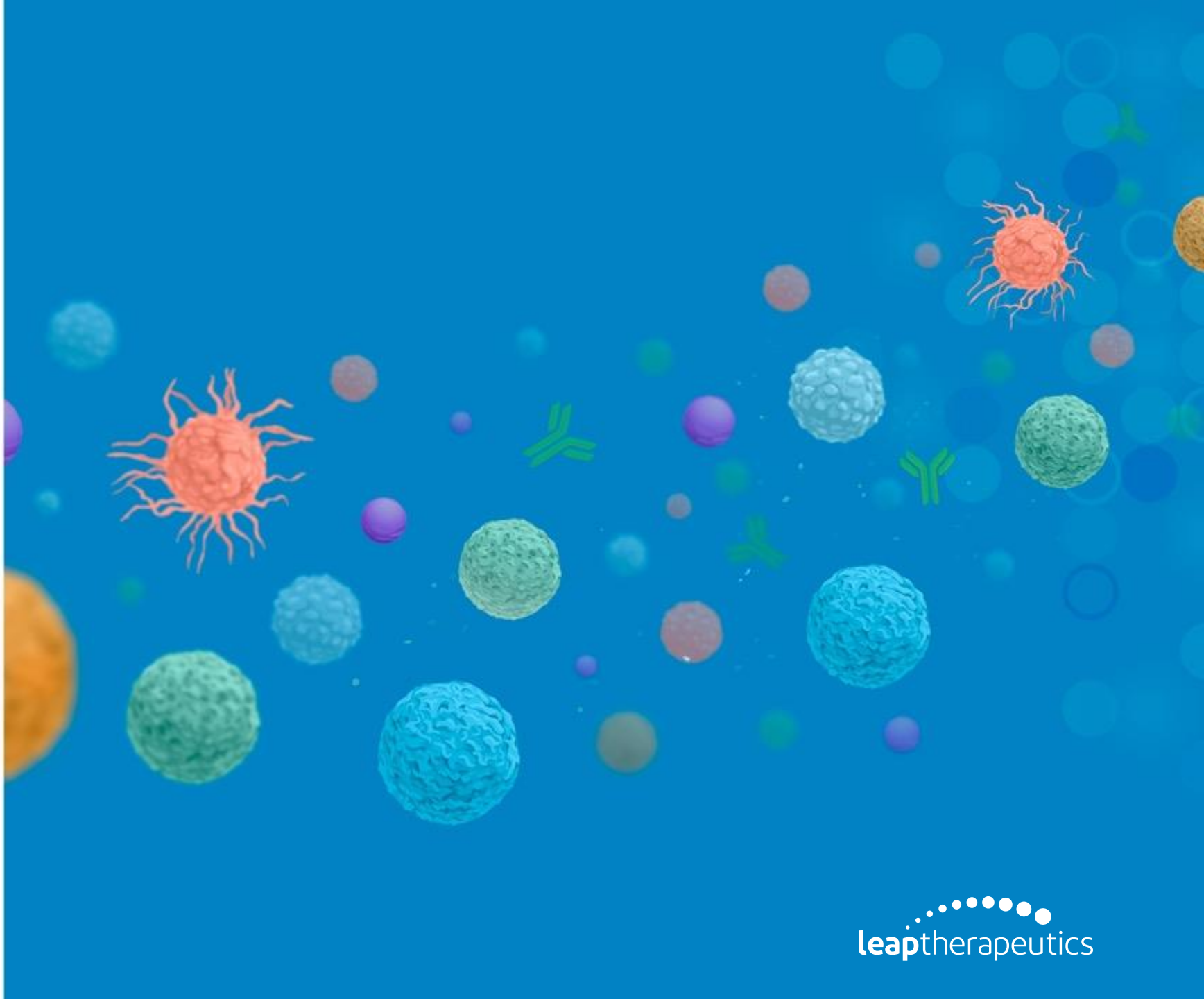
SIREXATAMAB (DKN-01)

Anti-DKK1 monoclonal antibody



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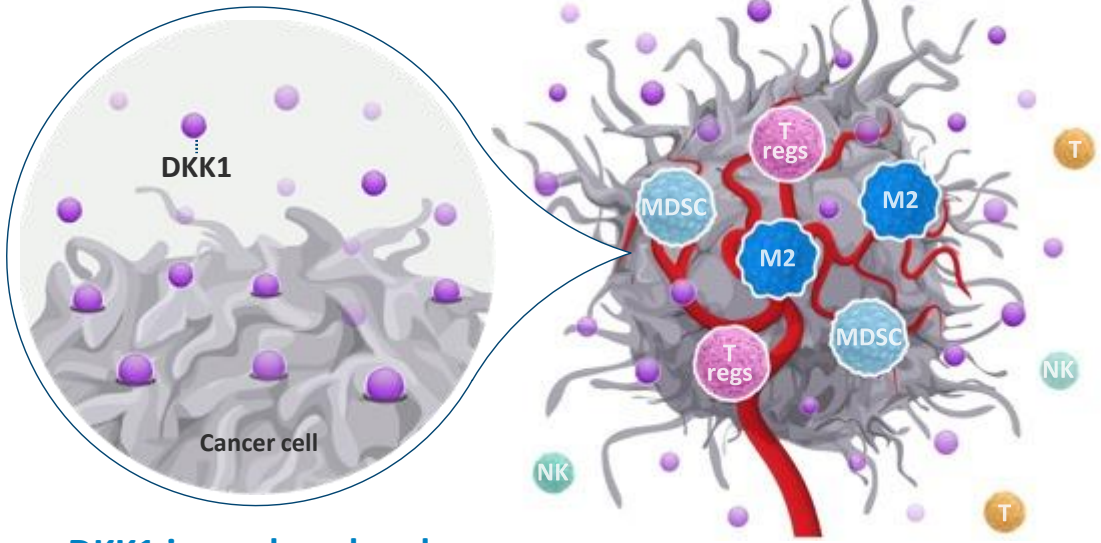
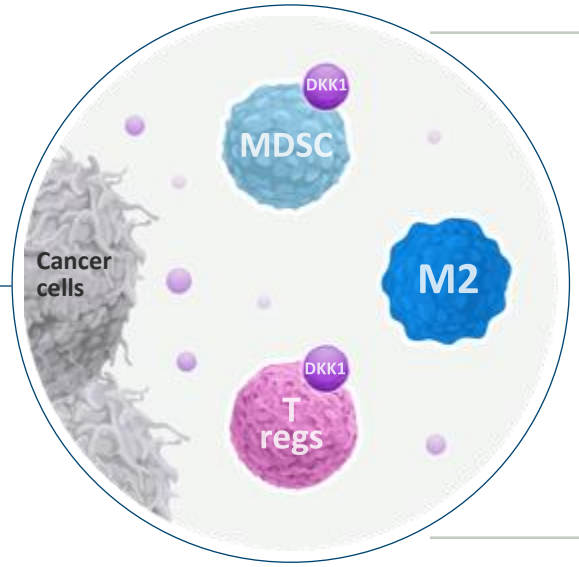
The role of DKK1 in cancer

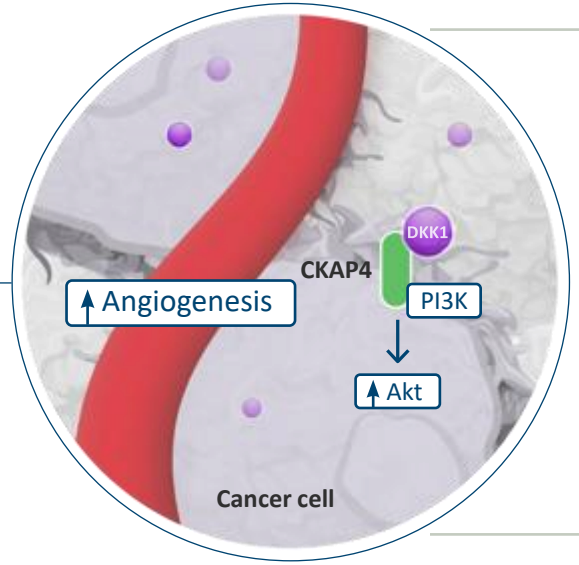


DKK1 is produced and secreted by cancer cells, and functions on several tumor pathways and nearby immune cells.



Enhances the suppressive activity of MDSCs and M2 macrophages.

Reduces NK cell activity and T-cell infiltration.



Promotes angiogenesis by increasing the number and size of blood vessels.

Promotes activation of Akt by direct signaling through CKAP4 and PI3 kinase.

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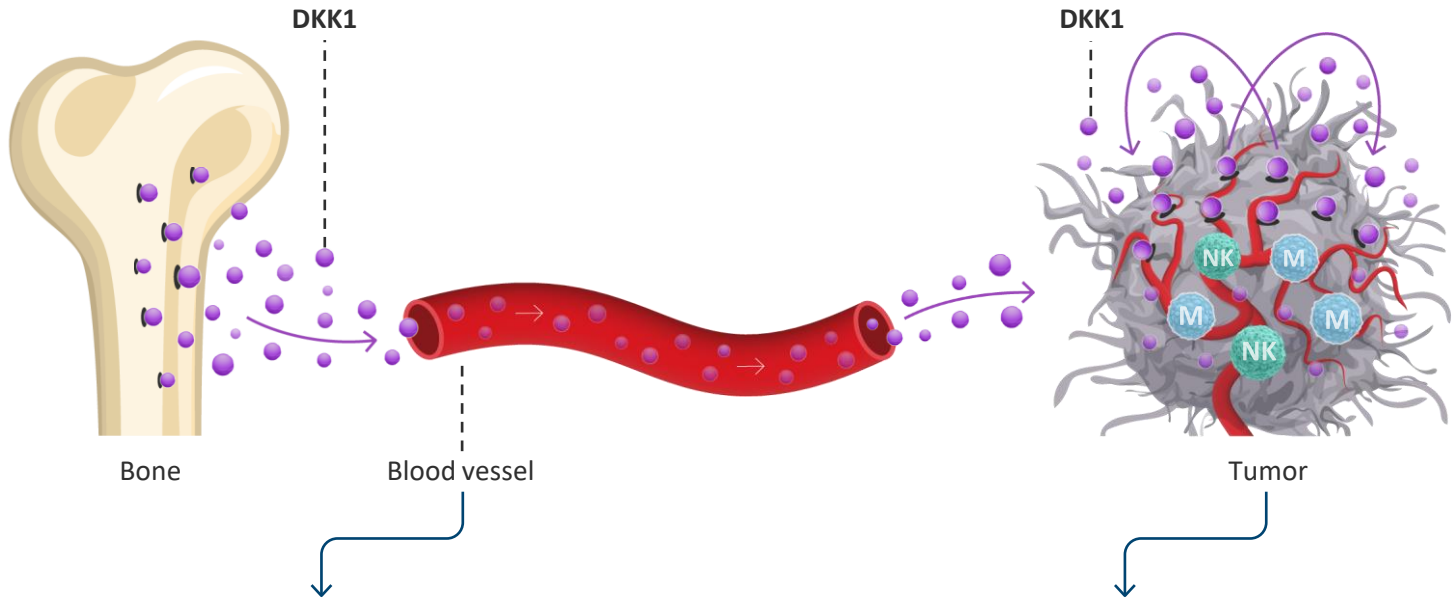
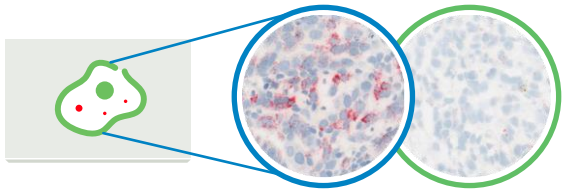
DKK1 production from multiple sources can drive tumor growth



DKK1 protein in circulation is measured by ELISA

ELISA
Enzyme-Linked Immunosorbent Assay

DKK1 RNA from the tumor is measured by RNAscope



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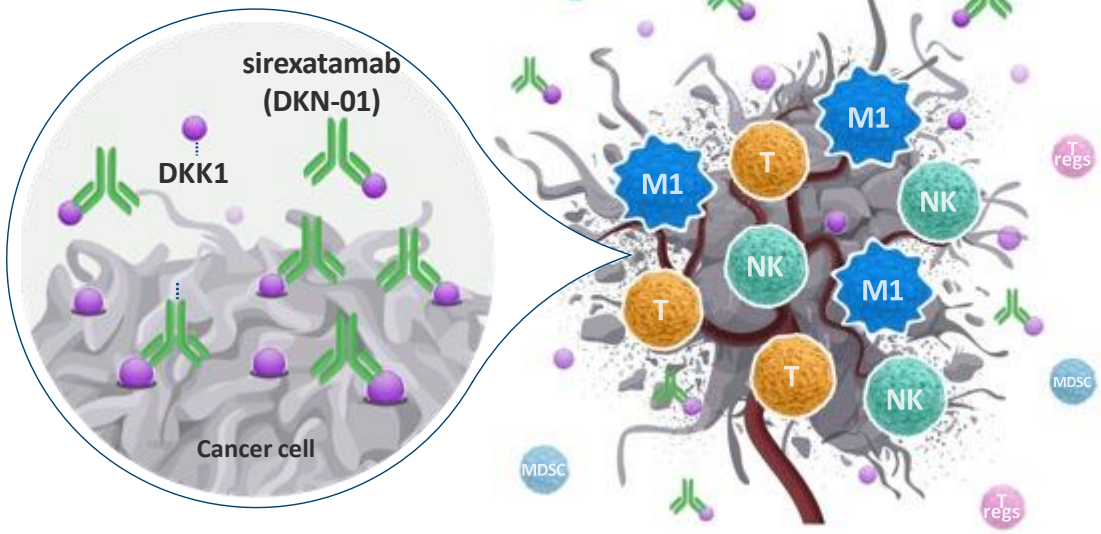
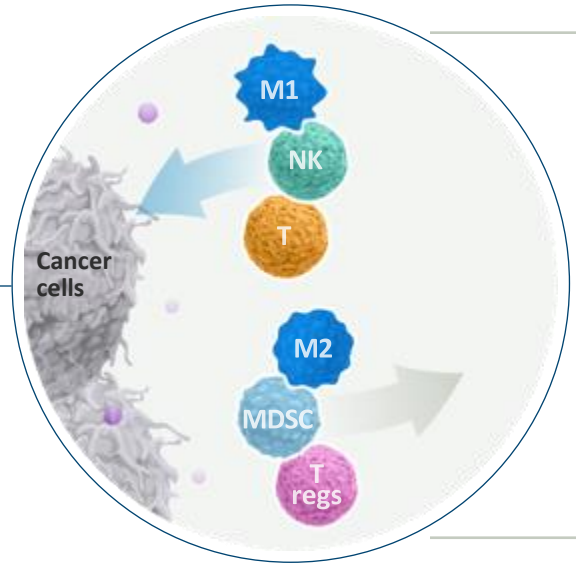
Activity of sirexatamab (DKN-01) to treat cancer

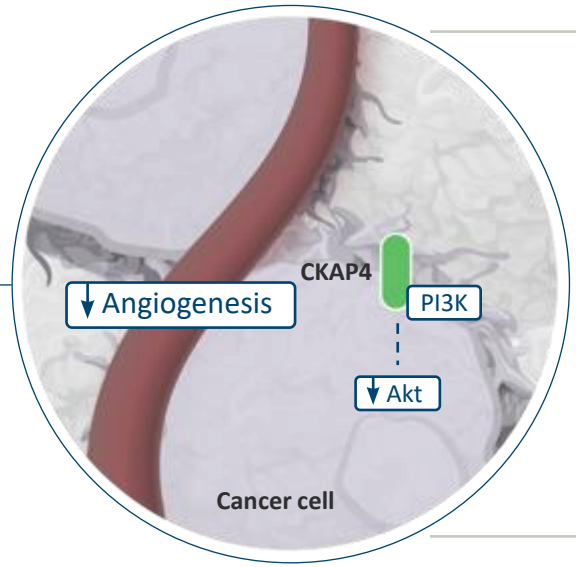


Sirexatamab (DKN-01) treatment neutralizes DKK1 and stimulates an immune mediated anti-tumor response.



Activates NK cells, reprograms macrophages into the tumor-attacking M1 subtype and promotes T cell infiltration.

Reduces MDSCs and tumor suppressive M2 macrophages in the TME.



Reduces angiogenesis and inhibits pro-oncogenic PI3K/AKT signaling.

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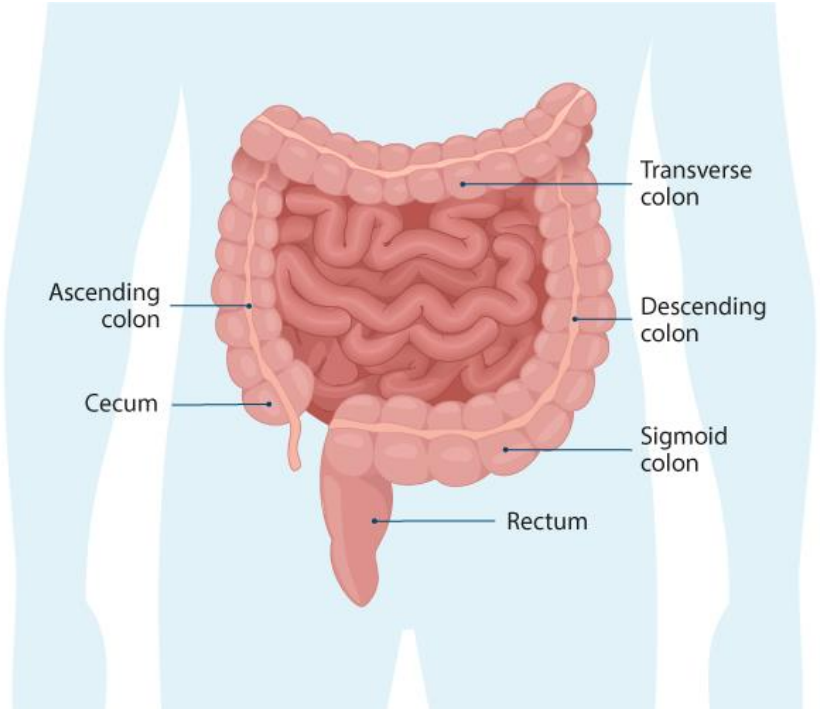
SIREXATAMAB (DKN-01)

Colorectal cancer development

Colorectal cancer background



- Includes right colon (cecum, ascending and transverse colon) and left colon (descending colon, sigmoid, and rectum)
- When symptoms appear, such as rectal bleeding, anemia, or abdominal pain, most patients already have advanced stage disease where cancers are aggressive and incurable
- Third most frequent cancer globally and the second leading cause of cancer-related death
- Globally, nearly 2,000,000 new cases in 2020, with nearly 1,000,000 deaths.
- In the US, estimated that there will be approximately 150,000 cases each year, resulting in more than 50,000 deaths.

Source: WHO Globocan 2020, American Cancer Society

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Significant unmet needs in 2L patients

Bevacizumab benchmark studies demonstrate need for new options for today's heterogeneous second-line patient population

Treatment	Bevacizumab + Chemo	Bevacizumab + Chemo	Bevacizumab + Chemo*
Study	ML18147	E3200	SLAVE
Population	Bevacizumab-experienced	Bevacizumab-naïve	EGFR-experienced
👤	404	286	228
ORR	5.4%	22.7%	25.7%
PFS	5.7	7.3	7.1
OS	11.2	12.9	16.2

*SLAVE included N=198 left sided CRC patients. This subgroup has an ORR of 22.7%

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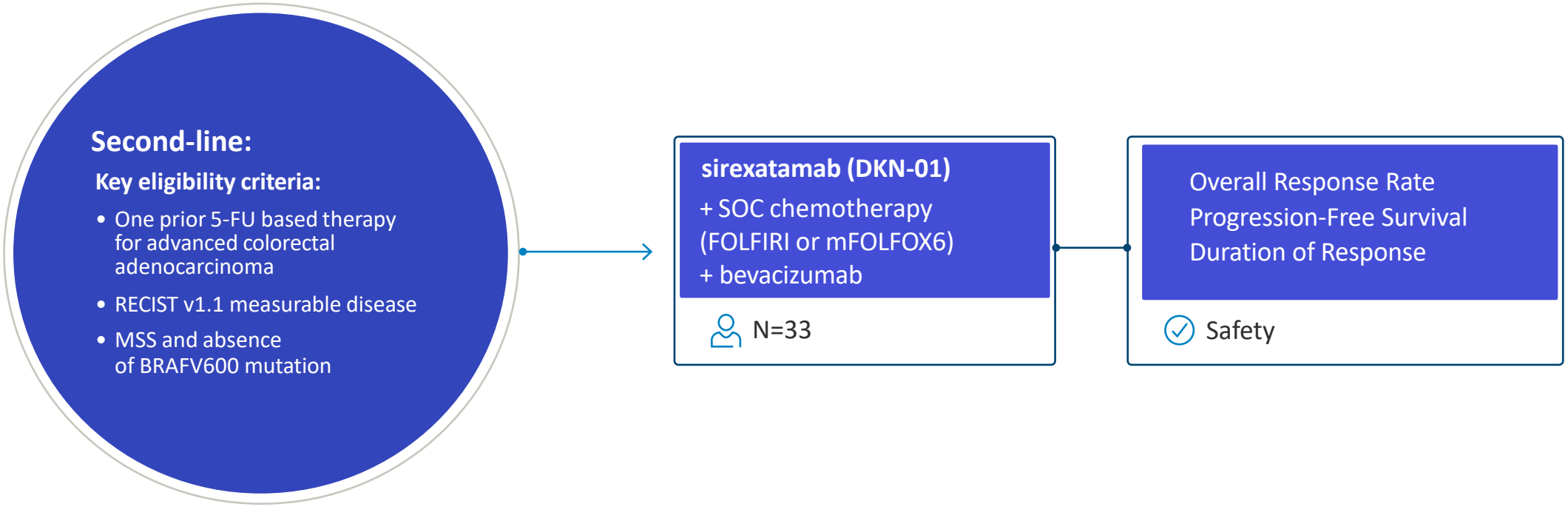
DeFianCe Part A study design

2L CRC
sirexatamab (DKN-01)
+ bevacizumab
+ chemotherapy

Randomized phase 2 study of FOLFIRI/FOLFOX and bevacizumab +/- sirexatamab (DKN-01) as second-line treatment of advanced colorectal cancer



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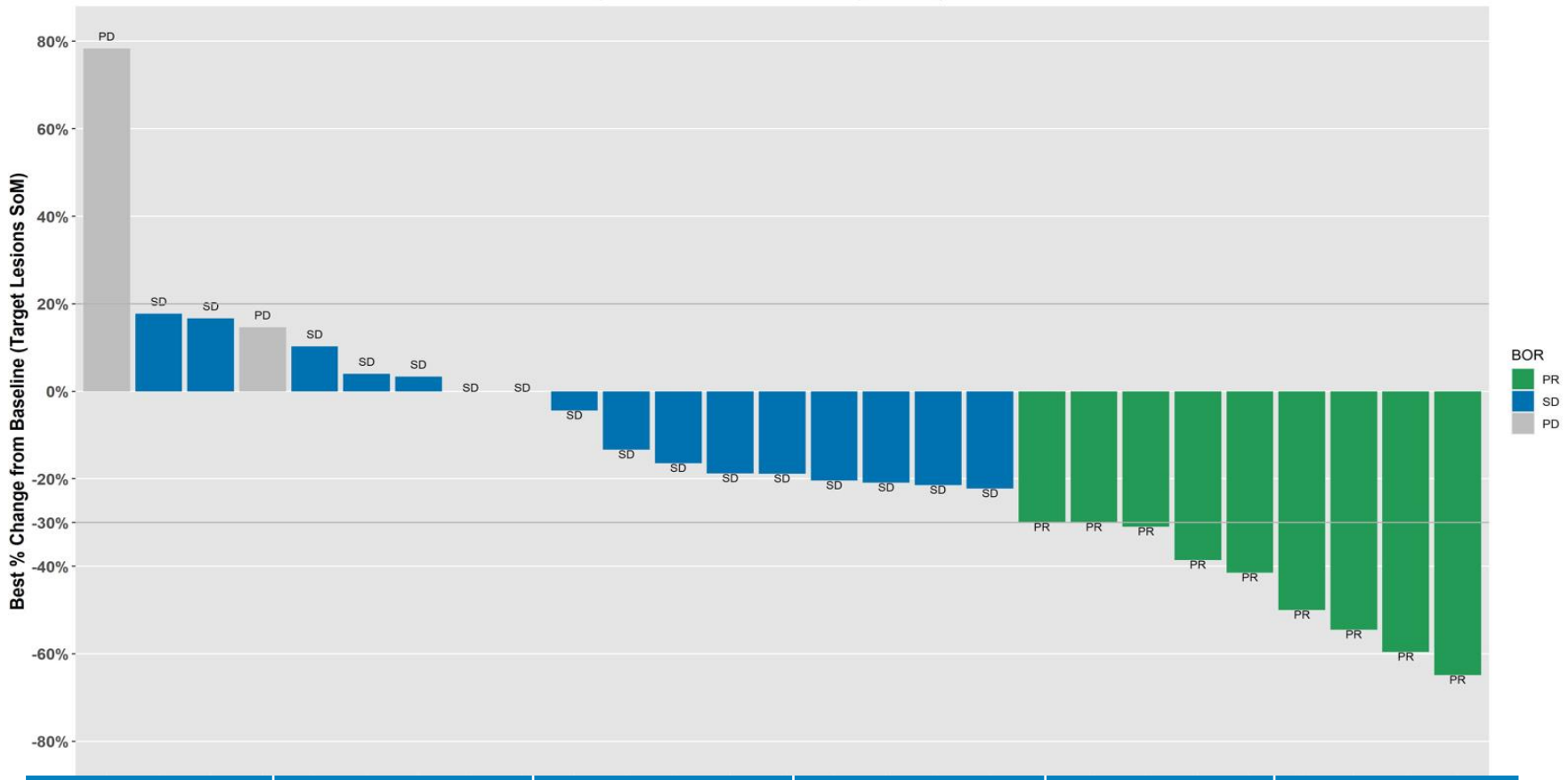
Overall response rate exceeded 20% target with high disease control rate

2L CRC
sirexatamab (DKN-01)
+ bevacizumab
+ chemotherapy



	Objective Response Rate (%)	Disease Control Rate (%)	Partial Response n (%)	Stable Disease n (%)	Progressive Disease n (%)
Overall, n=27	33	93	9 (33)	16 (59)	2 (7)

As of October 1, 2024

ORR in RE patients:
9/27 = 33%

DCR in RE patients:
25/27 = 93%

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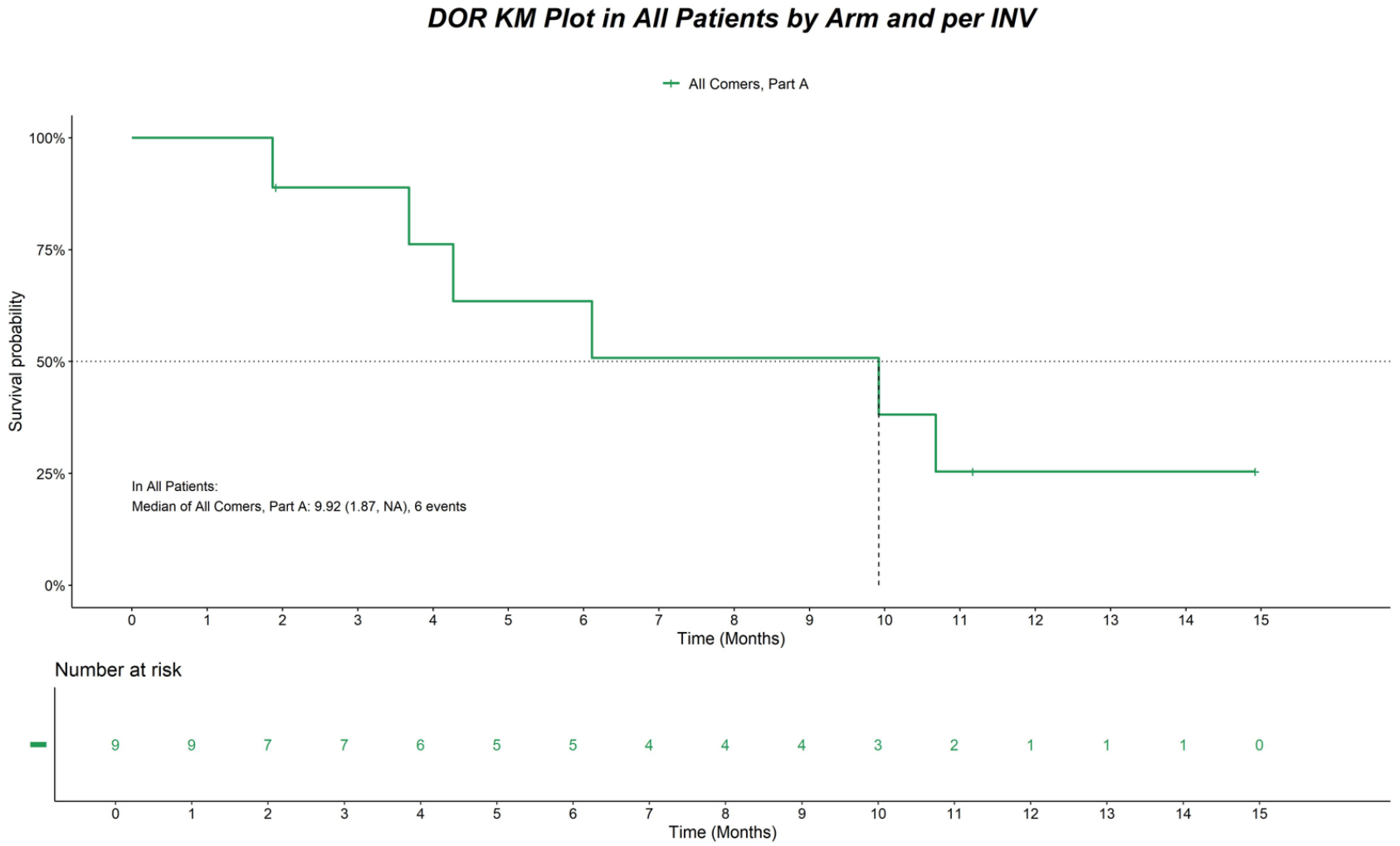
Duration of response

- Median DoR: 9.92 months

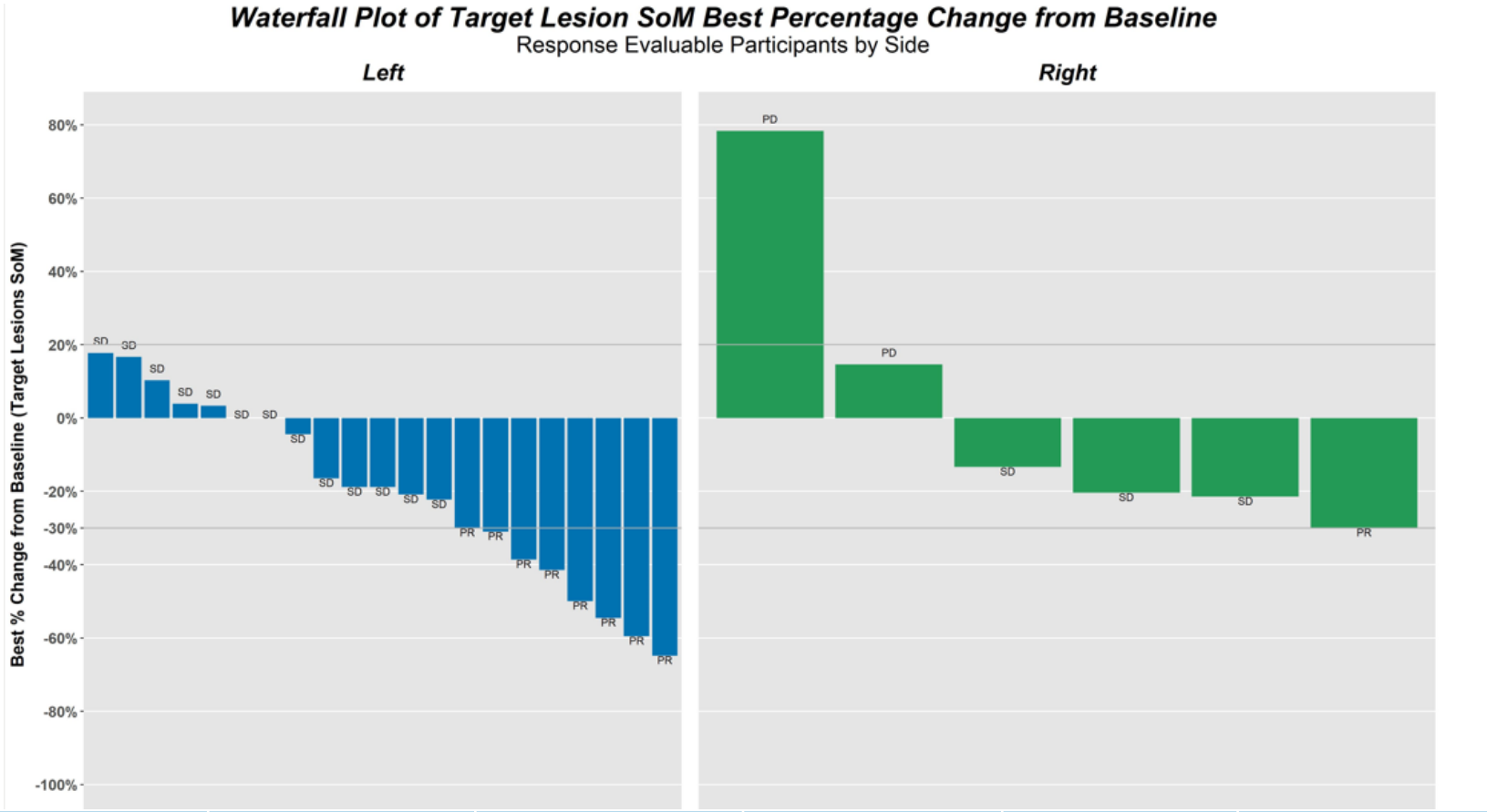
2L CRC
sirexatamab (DKN-01)
+ bevacizumab
+ chemotherapy



Data Cut-off: 2024-10-01

Best overall response based on tumor sidedness

2L CRC
sirexatamab (DKN-01)
+ bevacizumab
+ chemotherapy



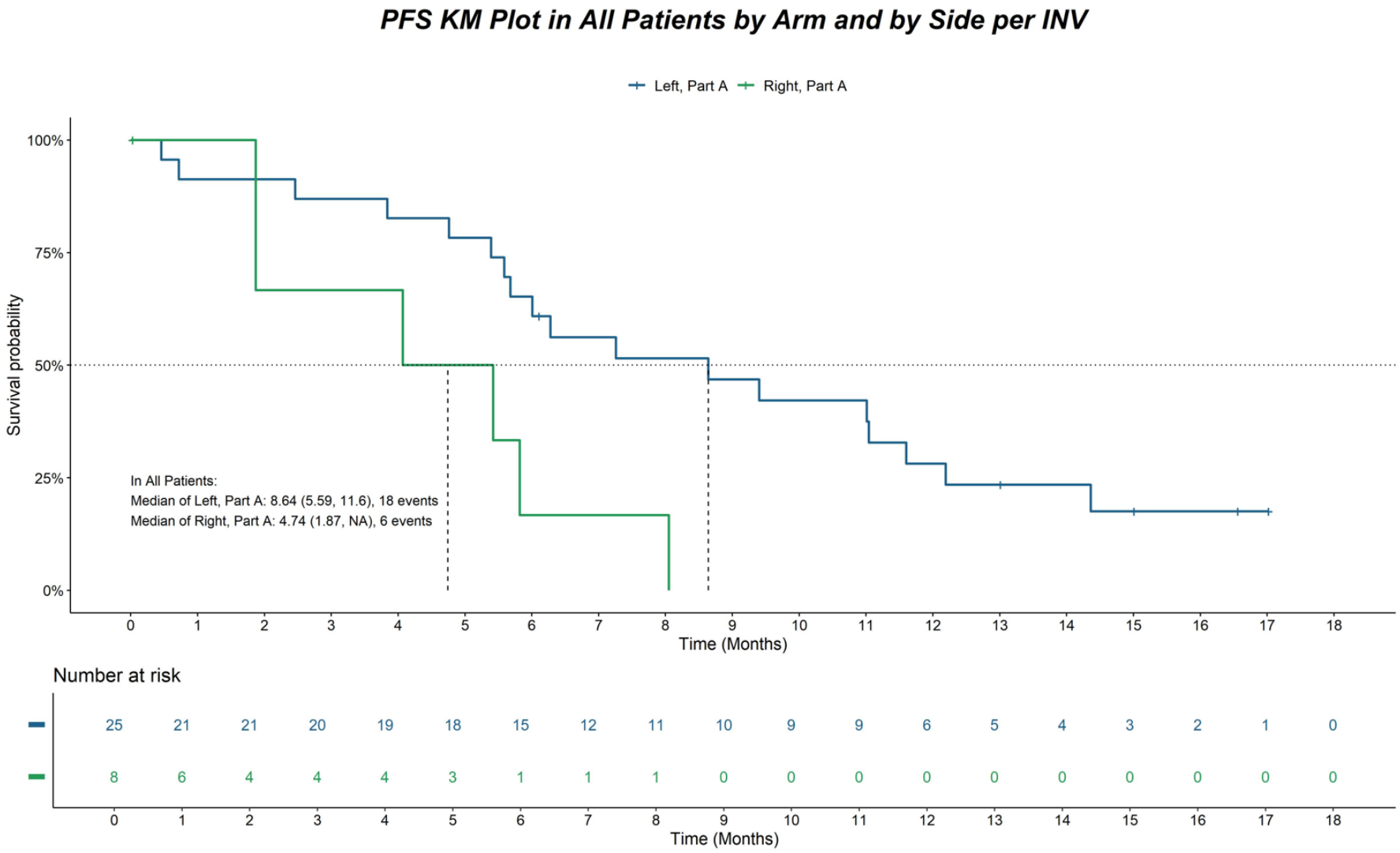
Overall, n=27	Objective Response Rate (%)	Disease Control Rate (%)	Partial Response n (%)	Stable Disease n (%)	Progressive Disease n (%)
Left (n=21)	38	100	8 (38)	13 (62)	0 (0)
Right (n=6)	17	67	1 (17)	3 (50)	2 (33)

As of October 1, 2024

Longer progression-free survival in patients with left-sided tumors

2L CRC
sirexatamab (DKN-01)
+ bevacizumab
+ chemotherapy

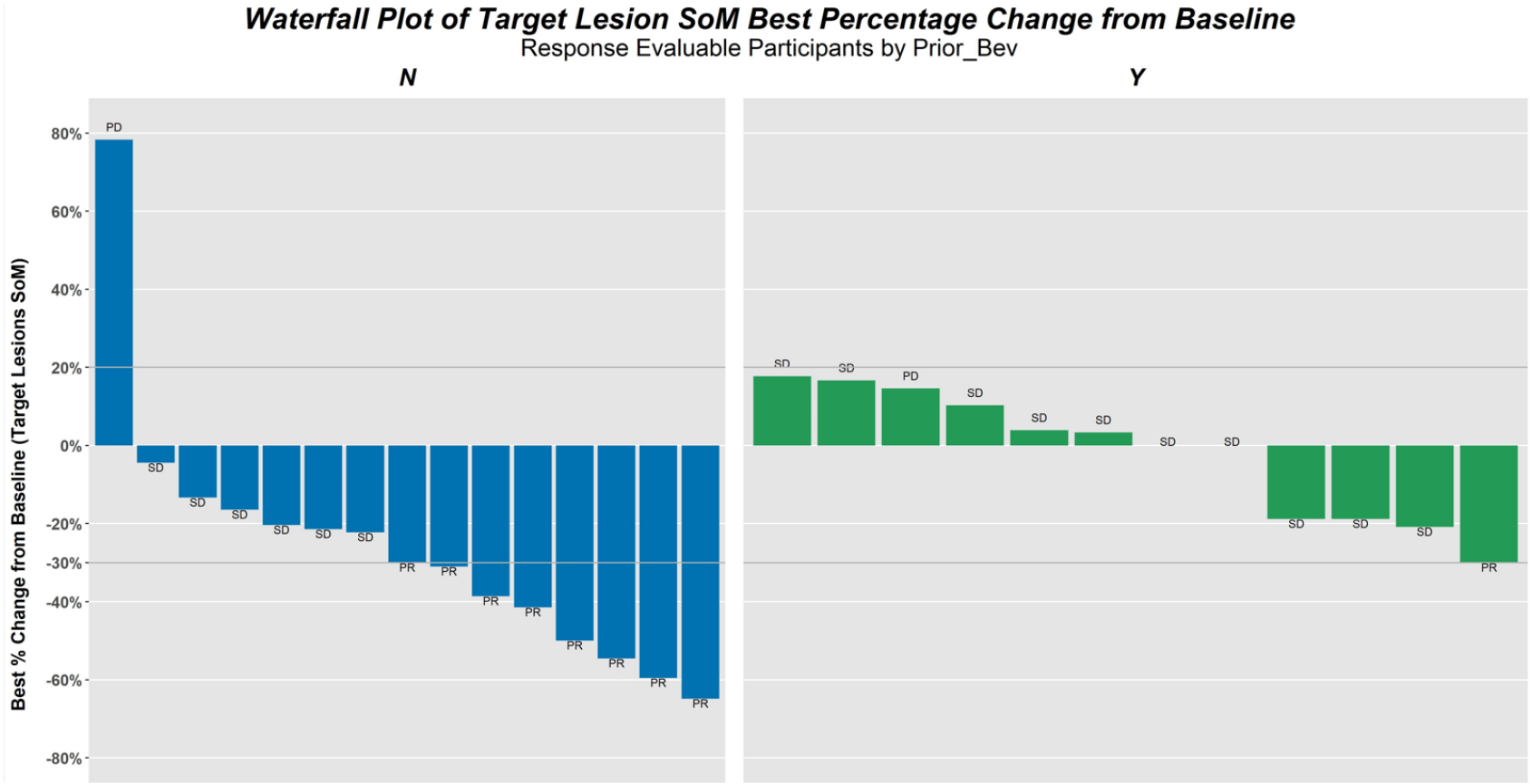
- Median PFS in left-sided tumors: 8.6 months



Data Cut-off: 2024-10-01

Best overall response based on prior bevacizumab exposure

2L CRC
sirexatamab (DKN-01)
+ bevacizumab
+ chemotherapy



Overall, n=27	Objective Response Rate (%)	Disease Control Rate (%)	Partial Response n (%)	Stable Disease n (%)	Progressive Disease n (%)
No Prior Bev (n=15)	53	93	8 (53)	6 (40)	1 (7)
Prior Bev (n=12)	8	83	1 (8)	10 (83)	1 (8)

As of October 1, 2024

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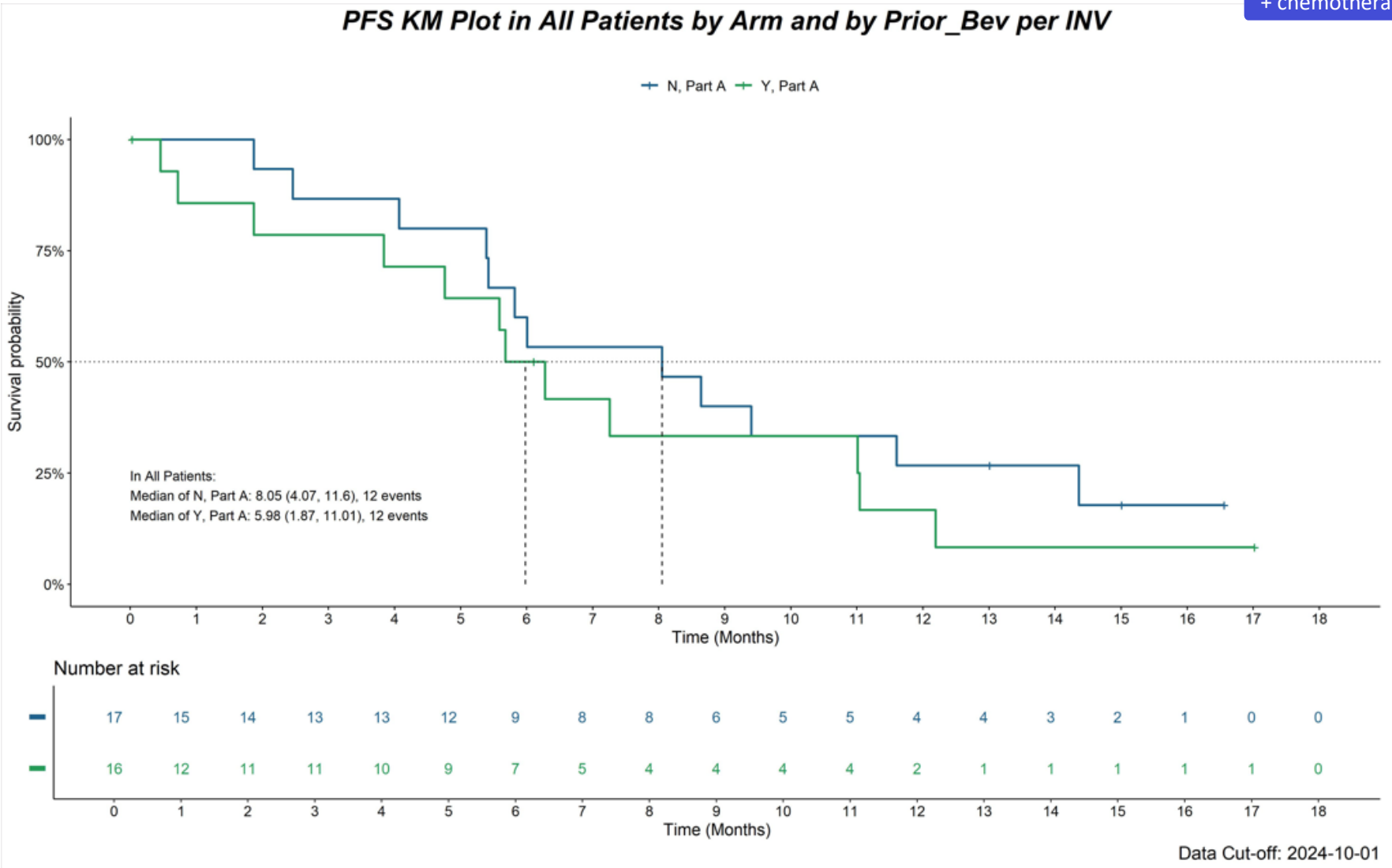
Progression-free survival
Bevacizumab exposure subgroup

2L CRC
sirexatamab (DKN-01)
+ bevacizumab
+ chemotherapy



Median PFS in bevacizumab naïve subgroup exceeds prior bevacizumab treated:
8.05 vs 5.98 months

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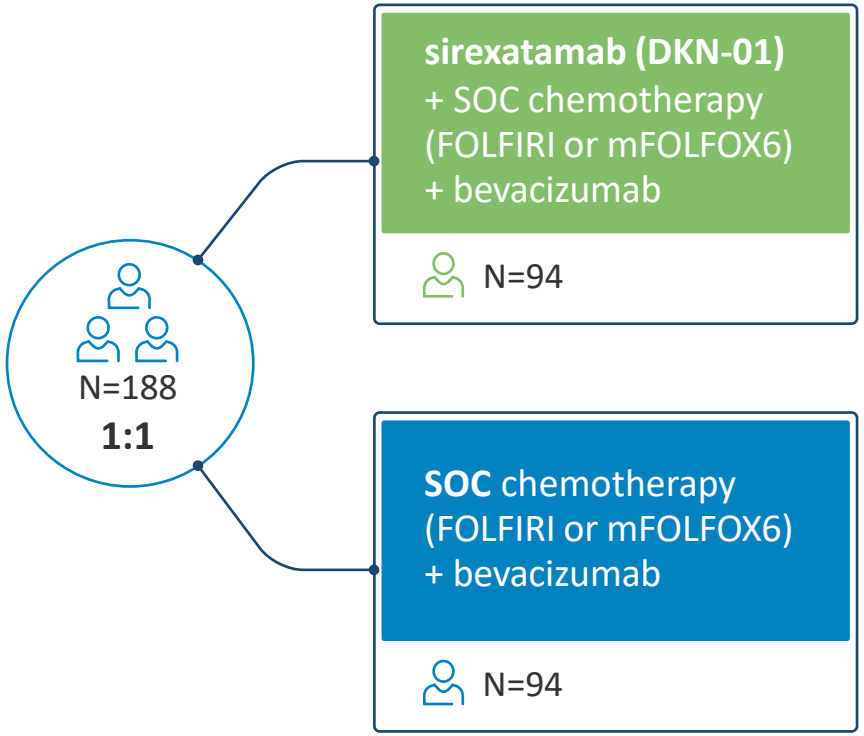
DeFianCe Part B study design

2L CRC
sirexatamab (DKN-01)
+ bevacizumab
+ chemotherapy

Randomized phase 2 study of FOLFIRI/FOLFOX and bevacizumab +/- sirexatamab (DKN-01) as second-line treatment of advanced colorectal cancer

Key eligibility criteria:

- One prior 5-FU based therapy for advanced colorectal adenocarcinoma
- RECIST v1.1 measurable disease
- MSS and absence of BRAFV600 mutation



- **Primary objective:**
  PFS, left-side and all
- **Secondary objectives:**
  – ORR
  – DoR
  – OS

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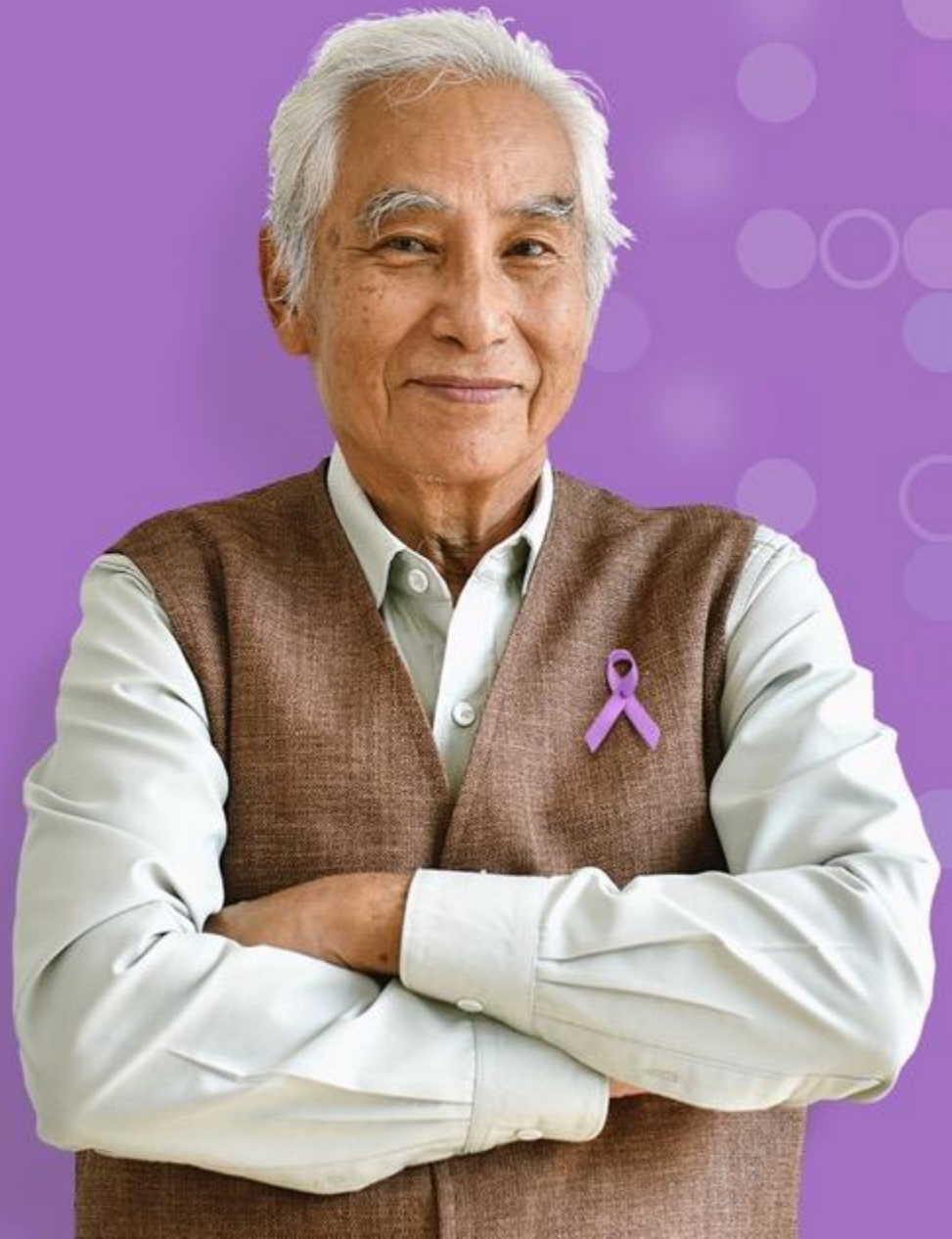
SIREXATAMAB (DKN-01)

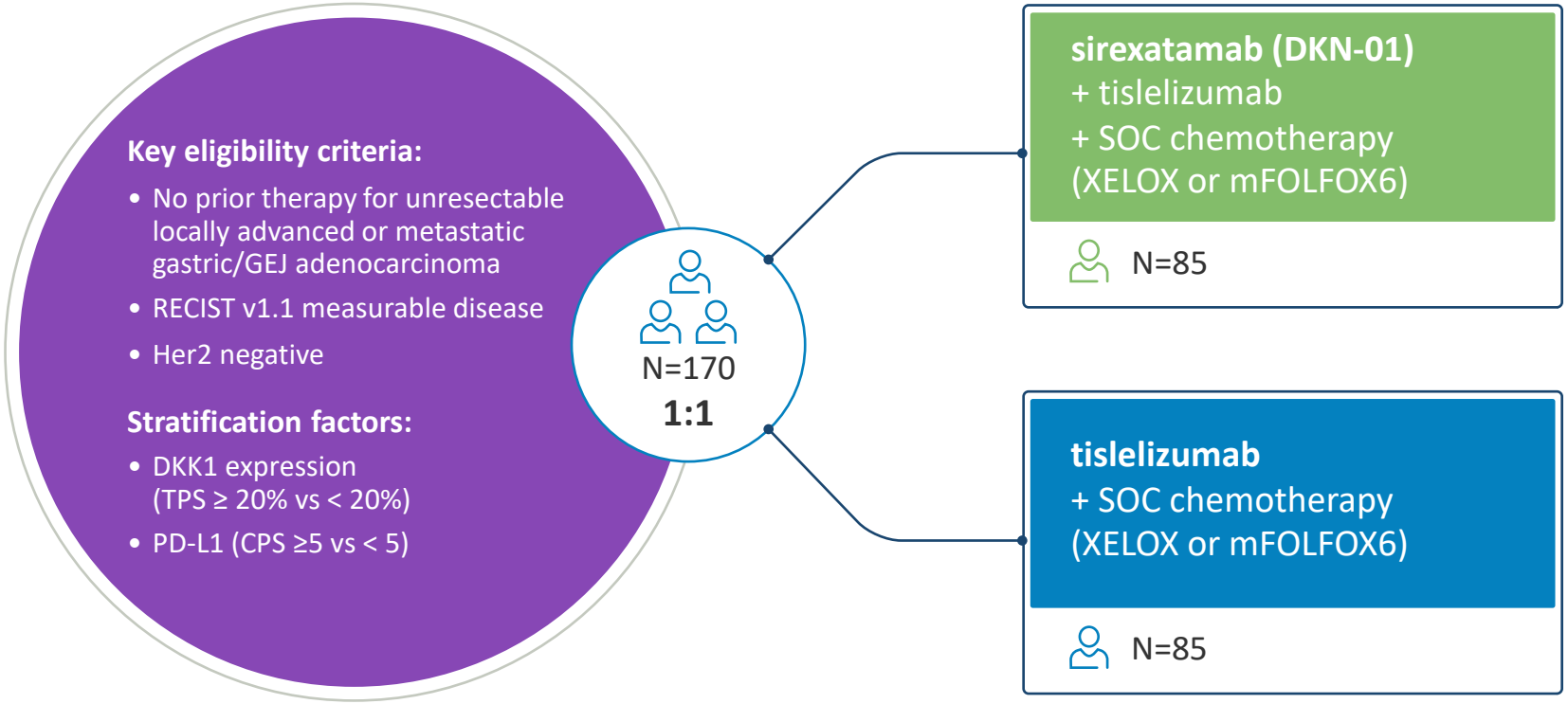
Gastric cancer development



DisTinGuish Part C study design

1L GEJ/GC
sirexatmab (DKN-01)
+ tislelizumab
+ chemotherapy

Randomized phase 2 study of FOLFIRI/FOLFOX and tislelizumab +/- sirexatamab (DKN-01) as first-line treatment of advanced GEJ/gastric cancer



Primary objective:
PFS, DKK1-high and all

Secondary objectives:
– ORR
– DoR
– OS

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Rationale-305 study: tislelizumab + chemotherapy in 1L GEJ/GC patients

	All Patients			North America & Europe			PD-L1 CPS < 1		
	Tislelizumab + Chemo N= 501	Control N= 496	HR (95% CI)	Tislelizumab + Chemo N= 125	Control N= 124	HR (95% CI)	Tislelizumab + Chemo N= 274	Control N= 272	HR (95% CI)
OS months (95% CI)	15.0 (13.6, 16.5)	12.9 (12.1, 14.1)	0.80 (0.69, 0.92)	11.0 (8.4, 13.9)	10.5 (8.1, 12.1)	0.71 (0.54, 0.94)	15.4 (8.4, 16.5)	13.8 (10.2, 17.8)	0.98 (0.64, 1.50)
DOR months (95% CI)	8.6 (7.9, 11.0)	7.2 (6.0, 8.5)		7.5 (4.4, 12.0)	5.0 (3.9, 6.7)		11.8 (4.3, NA)	18 (2.8, NA)	
PFS months (95% CI)	6.9 (5.7, 7.2)	6.2 (5.6, 6.9)	0.78 (0.67, 0.90)	5.6 (4.4, 7.0)	5.4 (4.3, 5.9)	0.84 (0.63, 1.11)	7.9 (5.6, 9.7)	6.9 (5.6, 15)	0.87 (0.54, 1.41)
ORR (%) (95% CI)	47.3% (42.9%, 51.8%)	40.5% (36.2%, 45.0%)		36.0% (27.6%, 45.1%)	31.5% (23.4%, 40.4%)		44.9% (32.9%,57.4%)	34.9% (21%, 50.9%)	

All patients and PD-L1 < TAP 1 from September 26, 2024 FDA Briefing Document
North American & Europe as presented at ASCO GI 2024

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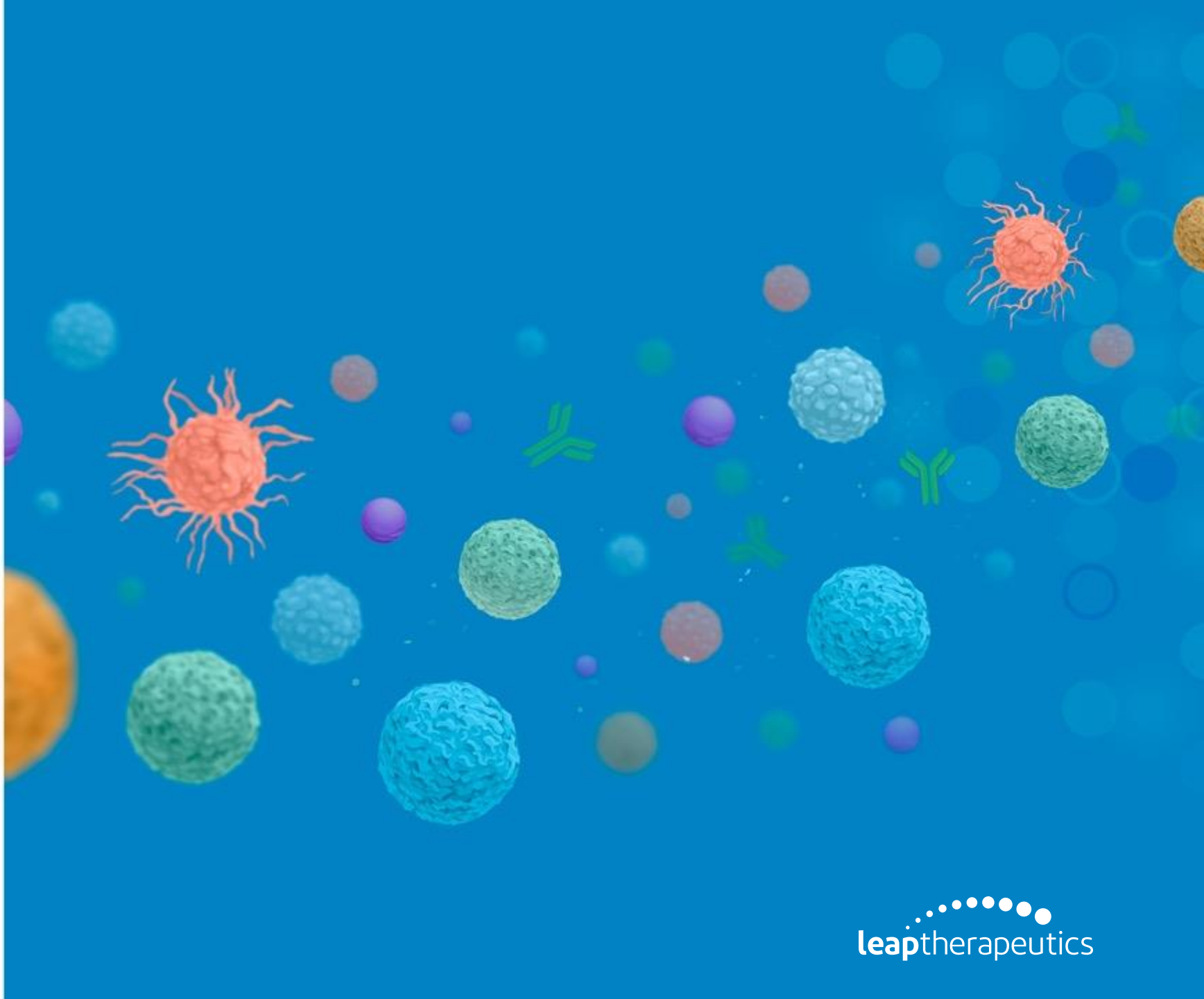
FL-501

Anti-GDF-15 monoclonal antibody



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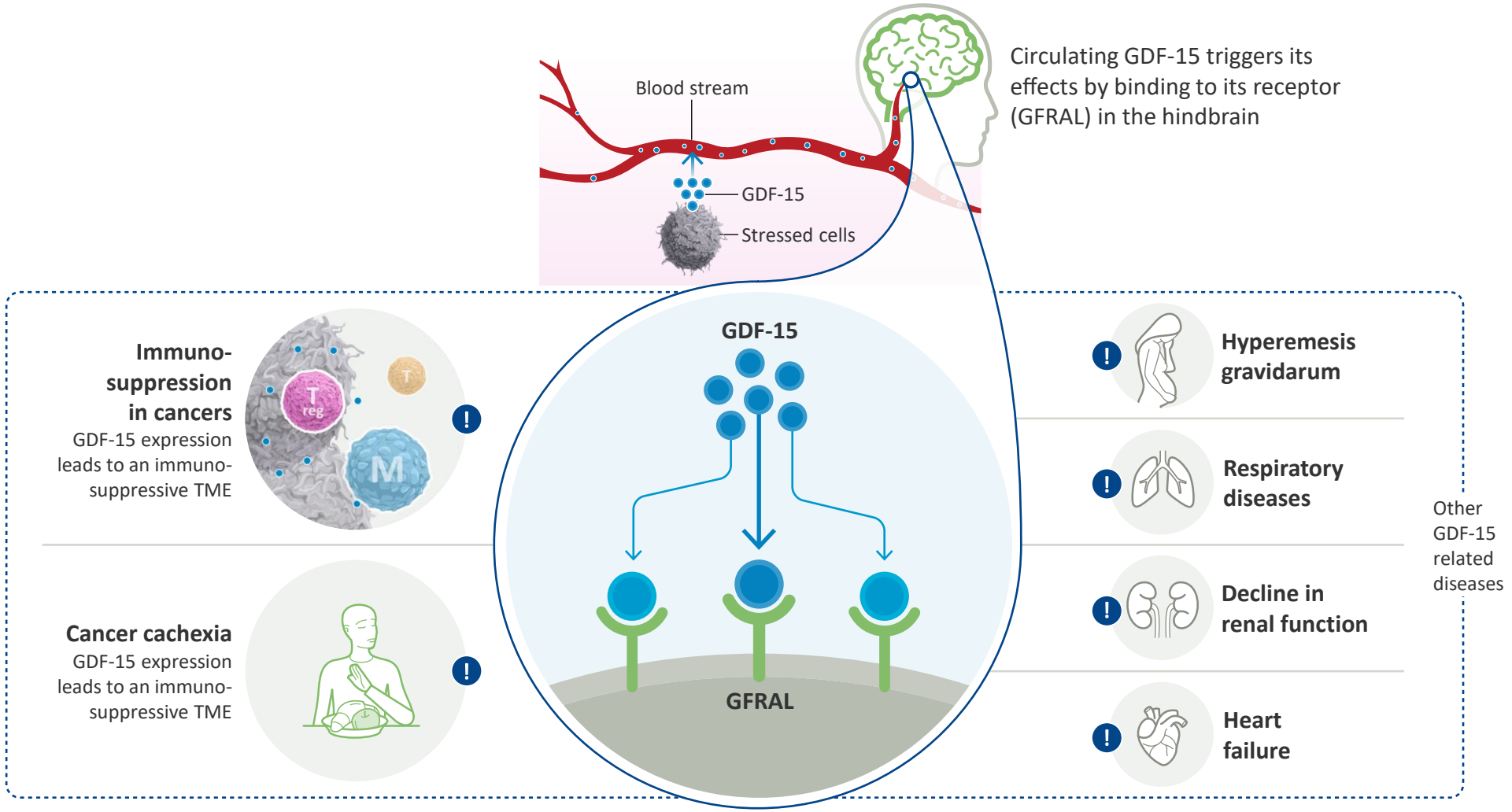
The role of GDF-15 in cachexia and cancer



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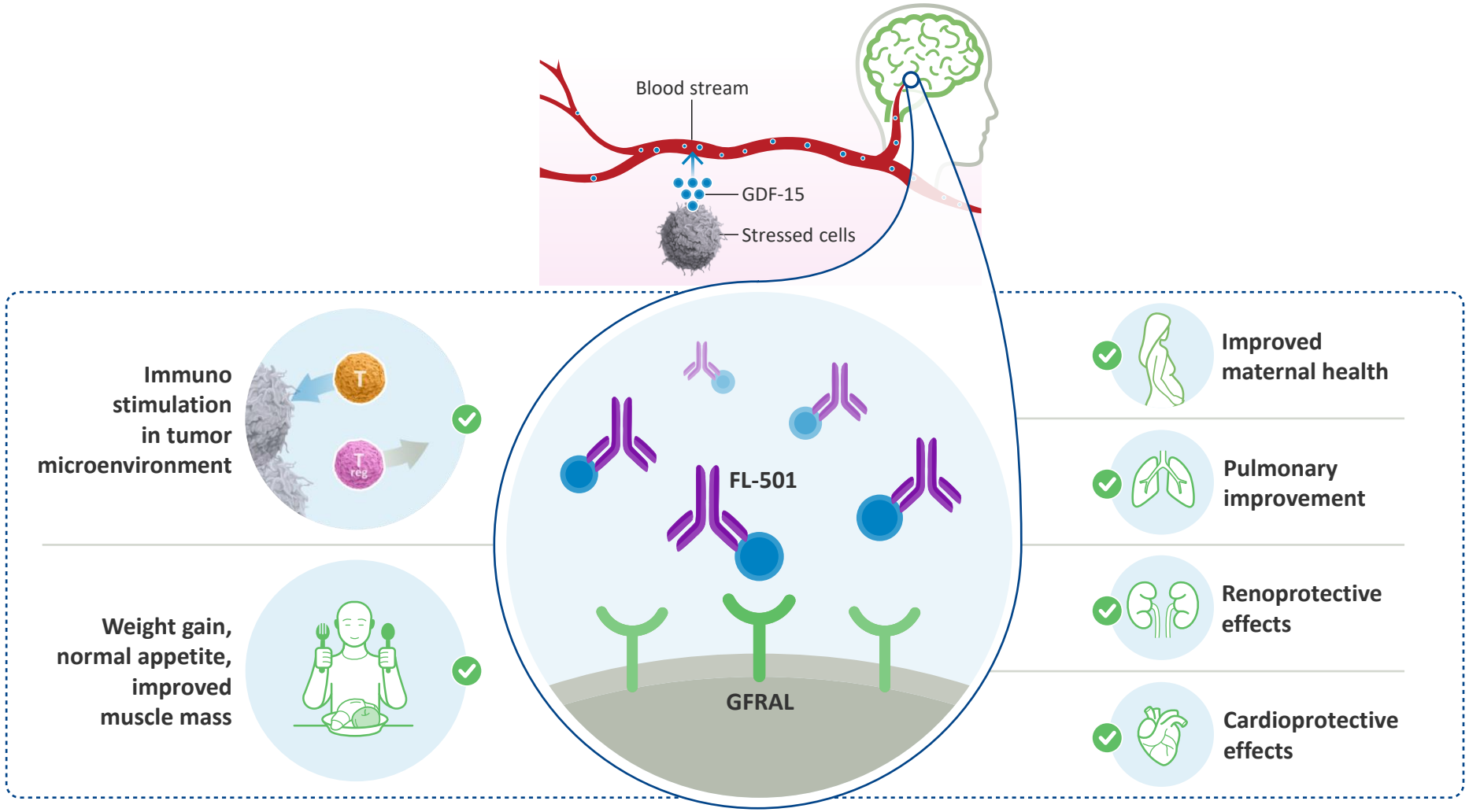
FL-501 mechanism of action



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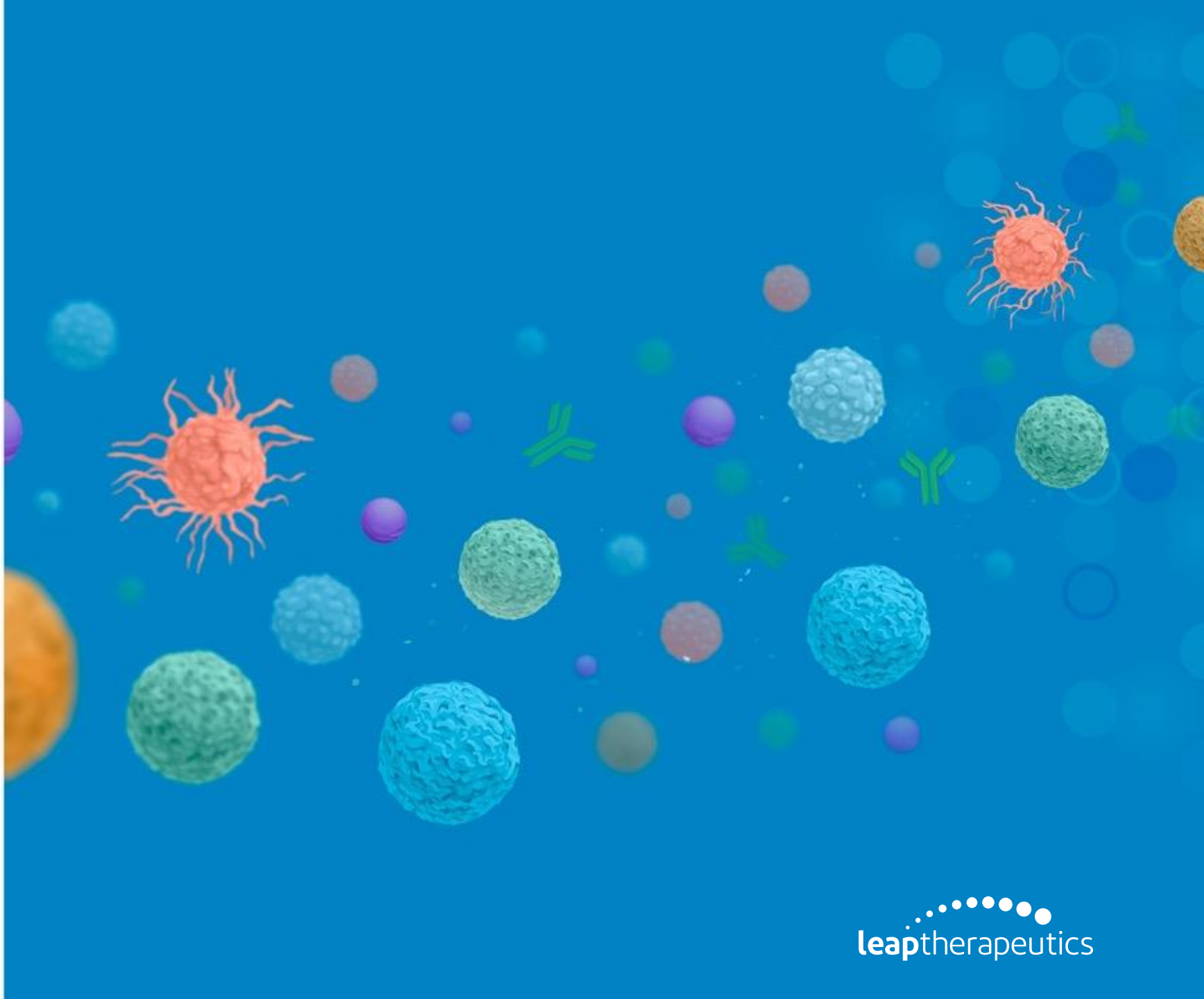
CORPORATE



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2025 Corporate Milestones

- Sirexatamab (DKN-01)
  - Initial data disclosure from both randomized controlled clinical trials expected in Q1 2025
  - DisTinGuish study in first-line gastric cancer: ORR and PFS in all patients, DKK1-high and PD-L1 low subgroups
  - DeFianCe study in second-line colorectal cancer: ORR in all patients, left-side and bevacizumab-naïve subgroups
  - Identify the Phase 3 development strategy

- FL-501
  - Manufacturing development initiated with goal of initiating a clinical trial in H1 2026
  - Preclinical data presentation expected in early Q2 2025

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