UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(D)
of the Securities Exchange Act of 1934

Date of report (Date of earliest event reported): **September 13, 2023**

Leap Therapeutics, Inc.
(Exact name of registrant as specified in its charter)

Delaware	**001-37990**	**27-4412575**
(State or other jurisdiction of incorporation)	(Commission File Number)	(IRS Employer Identification No.)

47 Thorndike Street, Suite B1-1 **Cambridge, MA** (Address of principal executive offices)	**02141** (Zip Code)

Registrant's telephone number, including area code: **(617) 714-0360**

N/A
(Former name or former address, if changed since last report)

Check the appropriate box below if the Form 8-K is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425).

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12).

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b)).

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c)).

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, par value $0.001	LPTX	Nasdaq Capital Market

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter)

Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 8.01. Other Events

On September 13, 2023, Leap Therapeutics, Inc. (the "Company") posted an updated corporate presentation on its website, www.leaptx.com. A copy of the presentation is filed as Exhibit 99.1 to this Current Report on Form 8-K and incorporated herein by reference.

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits.

Exhibit Number	Description
99.1	Leap Corporate Presentation
104	Cover Page Interactive Data File. (Embedded within the Inline XBRL document.)

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

LEAP THERAPEUTICS, INC.

Dated: September 13, 2023

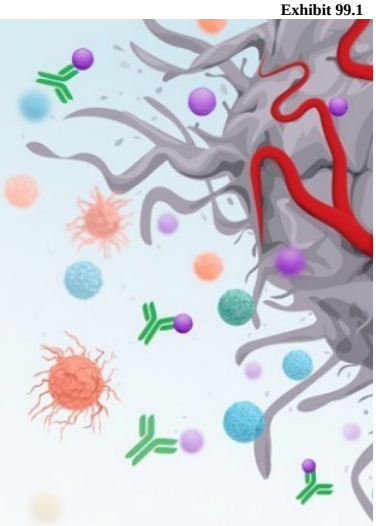
By: /s/ Douglas E. Onsi
Name: Douglas E. Onsi
Title: Chief Executive Officer and President

Exhibit 99.1

LEAP THERAPEUTICS

company presentation

September 13, 2023



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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.

This presentation does not constitute an offer to sell, or the solicitation of an offer to buy, any securities.

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Developing biomarker-targeted antibody therapies for cancer patients

Two clinical stage antibody programs – DKN-01 targeting DKK1 FL-301 targeting CLDN18.2

Upcoming multiple milestones from two randomized clinical trials

Biomarker strategy, focus on GI cancers

Cash runaway to mid H1 2025 with $91.4M at June 30, 2023

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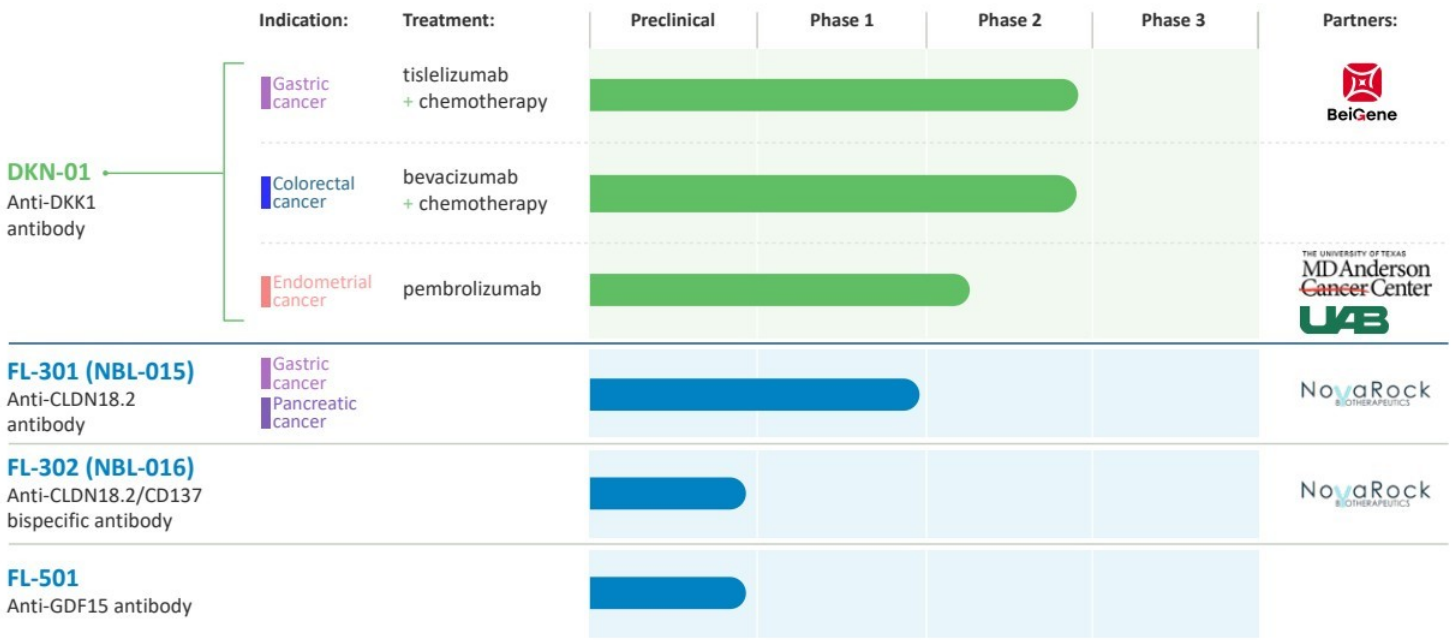
Pipeline



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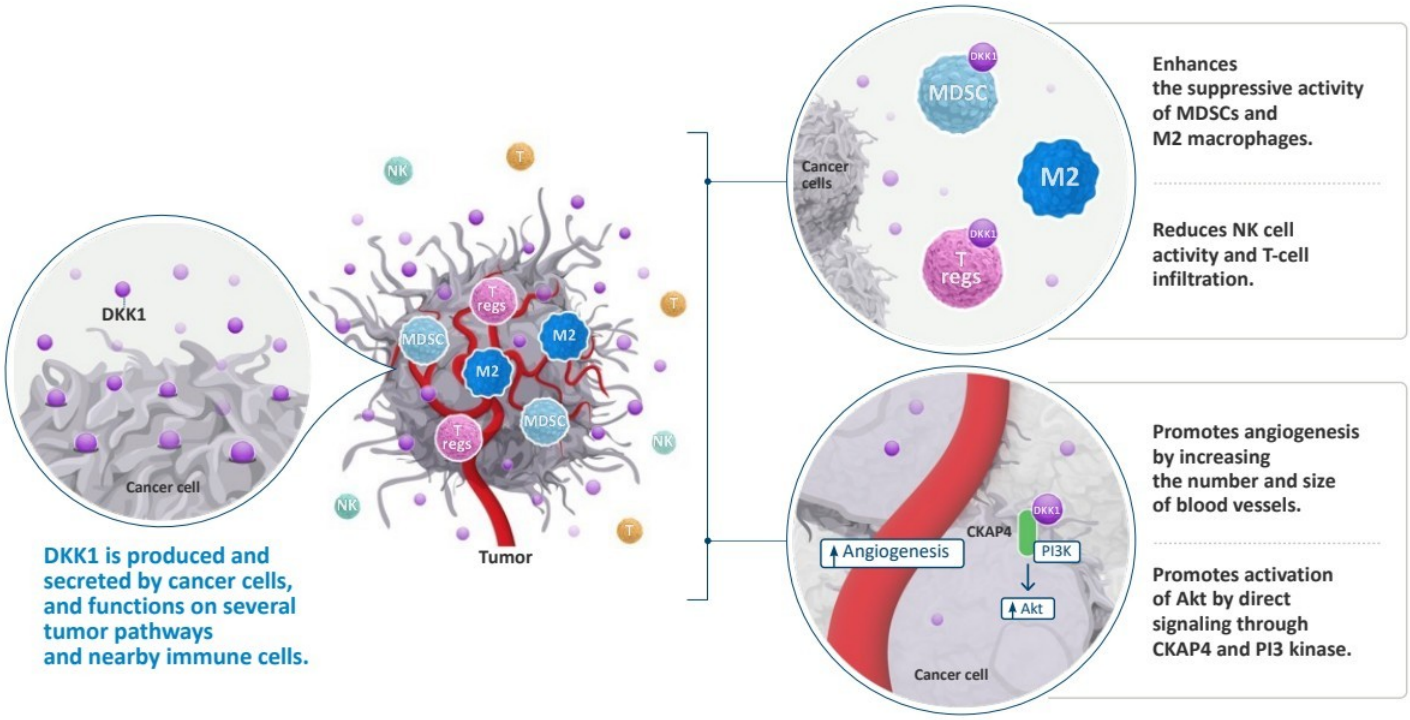
DKN-01

Anti-DKK1 monoclonal antibody

The role of DKK1 in cancer



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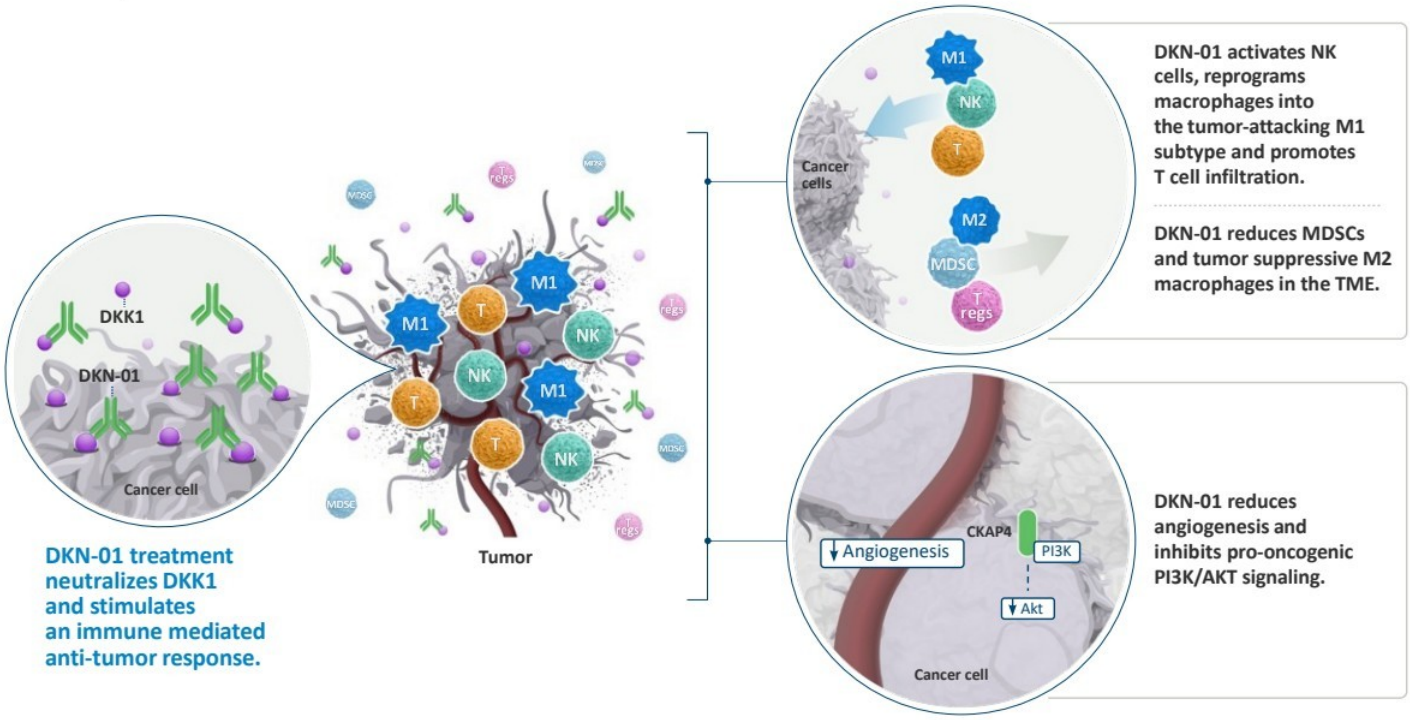
Activity of DKN-01 to treat cancer



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

DKN-01 activates NK cells, reprograms macrophages into the tumor-attacking M1 subtype and promotes T cell infiltration.

DKN-01 reduces MDSCs and tumor suppressive M2 macrophages in the TME.

DKN-01 reduces angiogenesis and inhibits pro-oncogenic PI3K/AKT signaling.

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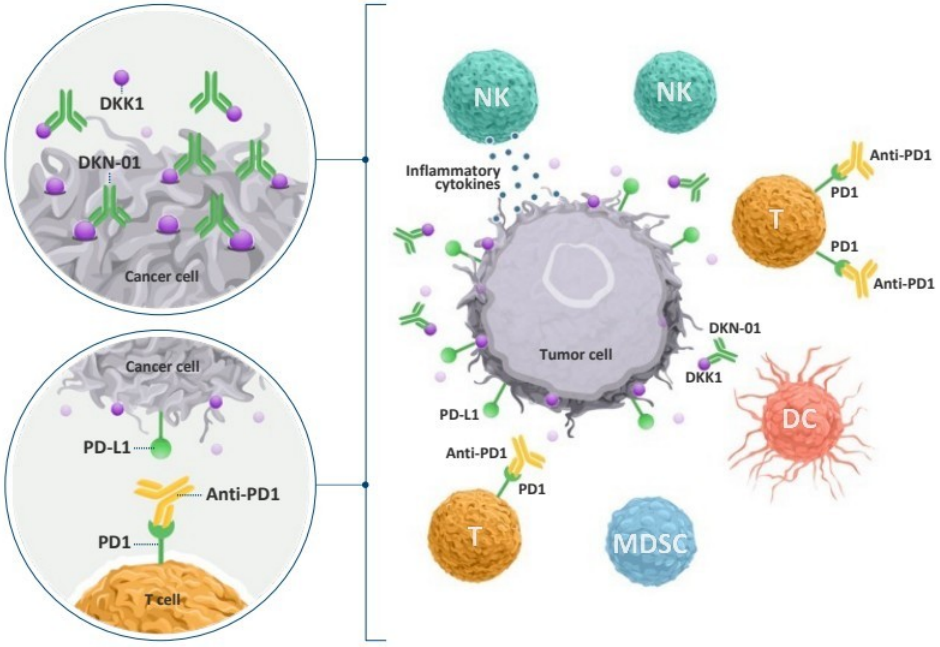
DKN-01 and anti-PD-1 cooperativity



DKN-01 targets innate immunity by activating NK cells, reprogramming Macrophages and inhibiting MDSCs, thus setting the stage for an enhanced adaptive immune response by anti-PD-1.

Promotes a pro-inflammatory M1 macrophage phenotype.

DKN-01 sensitizes tumors to anti-PD-1 therapies through upregulation of PD-L1.

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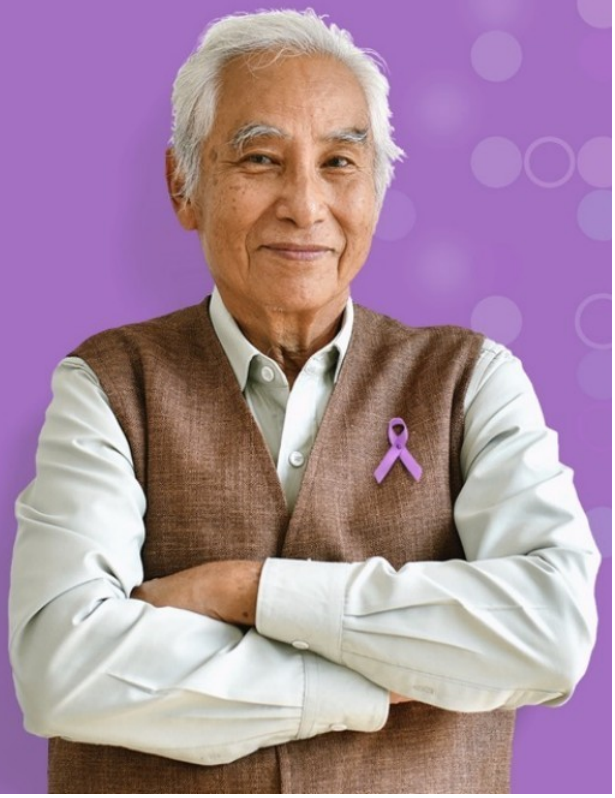
DKN-01

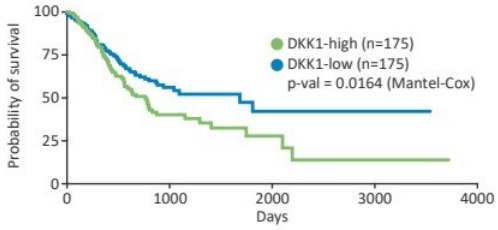
Gastric cancer development



DKK1-high levels are associated with poor survival in gastric cancer

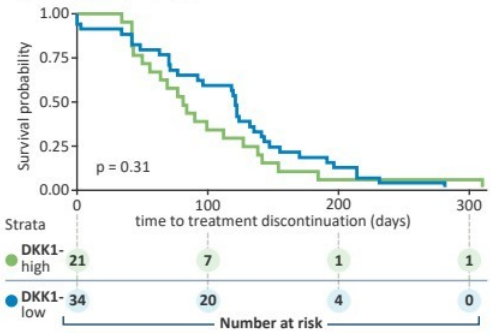
High levels of DKK1 correlate with shorter overall survival In gastric cancer

TCGA STAD dataset



DKK1-high is associated with poor response to first-line platinum + fluoropyrimidine based therapies in GEJ/gastric cancer patients

Collaboration with Tempus



DKN-01 single agent activity in heavily pretreated esophagogastric cancer patients

2L+ EGC
DKN-01

On Study 1 Year, Reduction -33.9%
Failed Prior anti-PD-L1 + IDOi

Baseline

4-month scan

Best Overall Response of 20 Evaluable Patients*	
Partial Response	2
Stable Disease	6
Progressive Disease	12

*By Blinded Independent Central Review

2 Monotherapy P

Clinical Benefit Ra
40%

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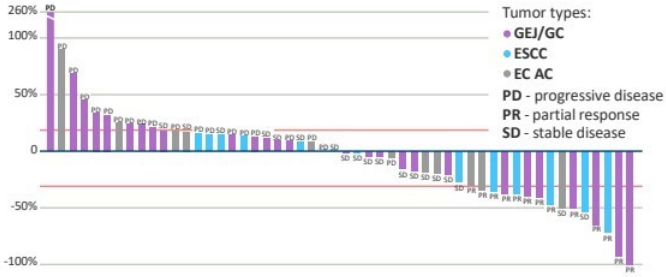
Clinical activity of DKN-01 plus paclitaxel or anti-PD-1 antibody

GEJ/GC
Historical data

DKN-01
+ paclitaxel
N=52
2L-8L esophagogastric pts



	Patients treated	Prior therapies	Overall response rate (ORR)	Disease control rate (DCR)
DKN-01 + paclitaxel	N=52	1-7	**25%**	**60%**

Strong broad activity in esophagogastric cancer in heavily pretreated patients

	Patients treated	PFS (months)	OS (months)	Overall response rate (ORR)	Disease control rate (DCR)
DKN-01 + paclitaxel	N=15	4.5	12.7	**46.7%**	**73.3%**

ORR in 2L patients is ~47%

DKN-01
+ pembro
N=31
2L+ GEJ/GC pts

location	Total (n)	PFS (mo)	OS (mo)	RE (n)	PR (n)	SD (n)	PD (n)	NE (n)	Overall response rate (ORR)	Disease control rate (DCR)
DKK1-high	n=11	5.1	7.3	10	5	3	2	1	**5 (50%)**	**8 (80%)**
DKK1-low	n=20	1.4	4	15	0	3	12	5	**0 (0%)**	**3 (20%)**

*DKK1-high ≥ upper tertile (35)

Achieved improved ORR, PFS, and OS in DKK1-high patients
Identified H-score threshold for DKK1 high/low expression

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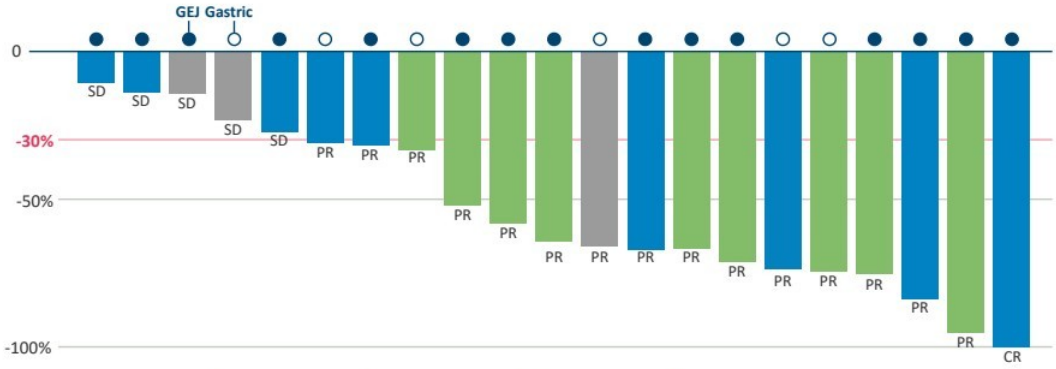
Response by DKK1 expression in first-line patients

1L GEJ/GC
DKN-01
+ tislelizumab
+ chemotherapy

Best % change in sum of diameters



	mITT* population N=22	**DKK1**-high N=10	**DKK1**-low N=9	**DKK1**-unknown N=3
CR - complete response	1 (5%)	0	1 (11%)	0
PR - partial response	15 (68%)	9 (90%)	5 (56%)	1 (33%)
SD - stable disease	5 (23%)	0	3 (33%)	2 (67%)
PD - progressive disease	0	0	0	0
NE - non-evaluable	1 (5%)	1 (10%)	0	0

All 9 of the evaluable DKK1-high patients had a partial response

1 PR went to curative surgery with pathological CR

73%
ORR in the mITT Population

(1 CR; 15 PR)

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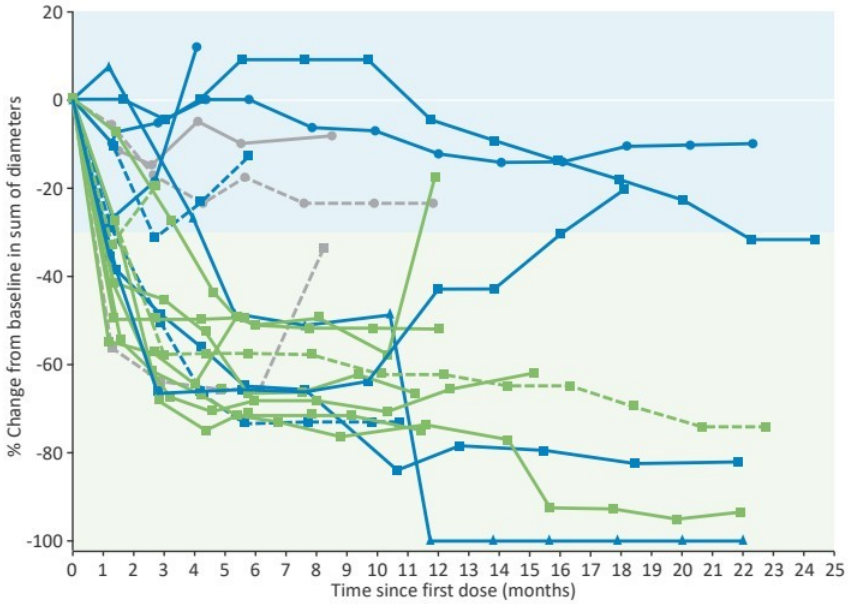
*mITT population includes all patients who received > 1 dose of DKN-01
As presented at ASCO 2023

Durability of clinical benefit by DKK1 expression

1L GEJ/GC
DKN-01
+ tislelizumab
+ chemotherapy

Best % change in sum of diameters



90%
ORR in DKK1-high patients

As presented at ASCO 2023

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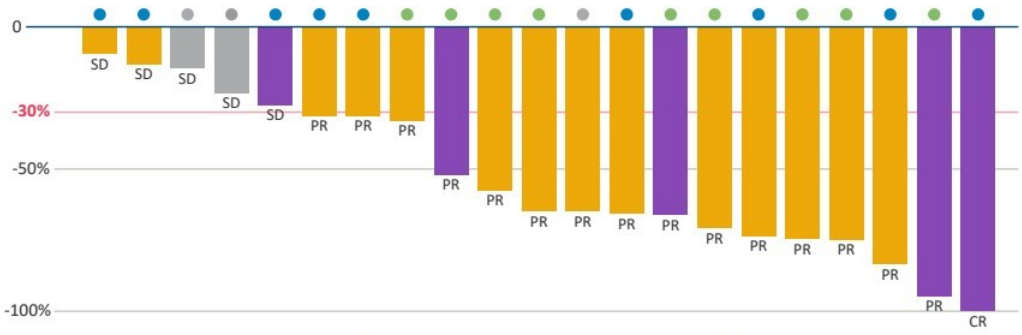
Response by PD-L1 expression

1L GEJ/GC
DKN-01
+ tislelizumab
+ chemotherapy

Best % change in sum of diameters



	PD-L1 CPS ≥5		PD-L1 CPS <5		
	DKK1-high N=4	**DKK1**-low N=2	**DKK1**-high N=6	**DKK1**-low N=7	**DKK1**-unknown N=1
CR - complete response		1 (50%)			
PR - partial response	3 (75%)	0	6 (100%)	5 (71%)*	1 (100%)
SD - stable disease	0	1 (50%)	0	2 (29%)	0
PD - progressive disease	0	0	0	0	0
NE - non-evaluable	1 (25%)	0	0	0	0
	N=6 **67% ORR**		N=14 **86% ORR**		

vCPS: visually-estimated combined positive score; PD-L1: programmed death-ligand 1
*Includes one pathologic CR
As presented at ASCO 2023

86%
ORR in PD-L1 low patients

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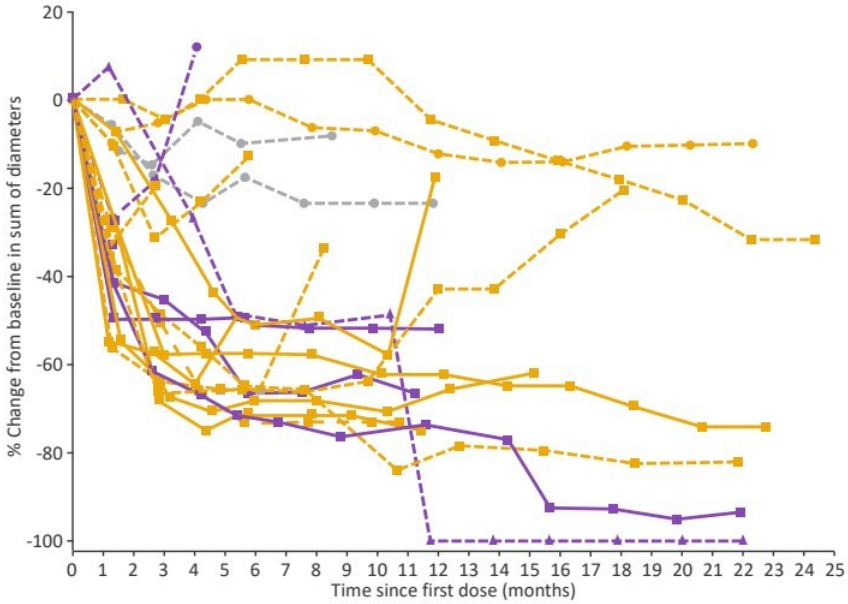
Durability of clinical benefit by PD-L1 expression

1L GEJ/GC
DKN-01
+ tislelizumab
+ chemotherapy

Best % change in sum of diameters



86%
ORR in PD-L1 Low patients

16 As presented at ASCO 2023

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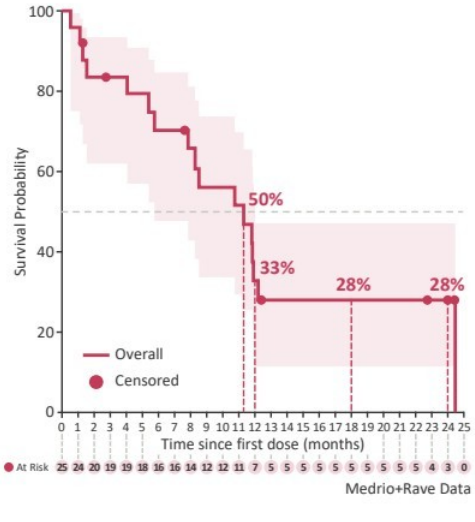
Progression-free survival

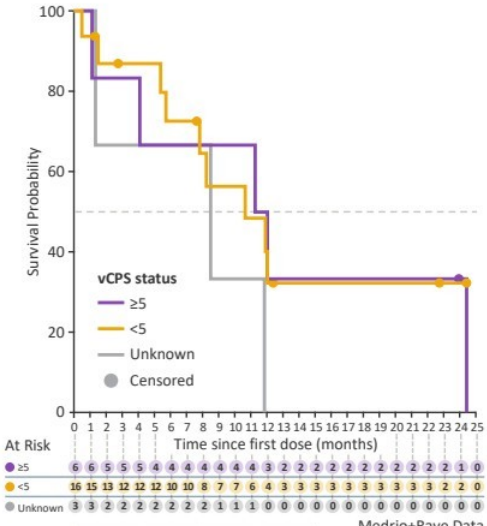
1L GEJ/GC
DKN-01
+ tislelizuma
+ chemothe

Overall Population



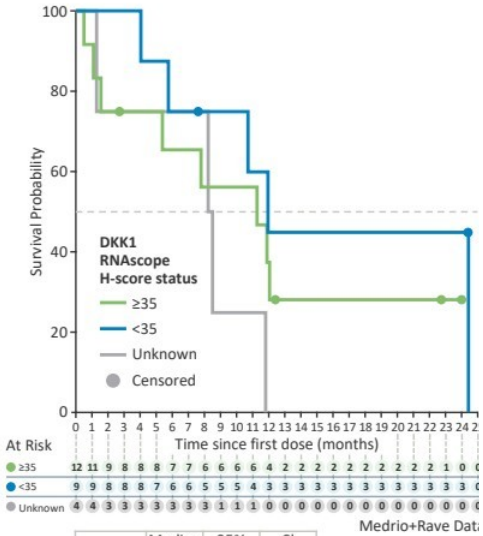
	Median	95%	CI
Overall	11.3	5.75	12.0

By PD-L1 Expression



vCPS	Median	95%	CI
≥5	11.6	1.12	NA
<5	10.7	5.39	NA
Unknown	8.51	1.31	NA

By DKK1 Expression



	Median	95%	CI
≥35	11.3	1.12	NA
<35	12.0	4.07	NA
Unknown	8.4	1.31	NA

DKK1-high: H-score ≥35; | DKK1-low: H-score <35 | PD-L1: Programmed Death-Ligand 1 | vCPS: Visually-Estimated Combined Positive Score

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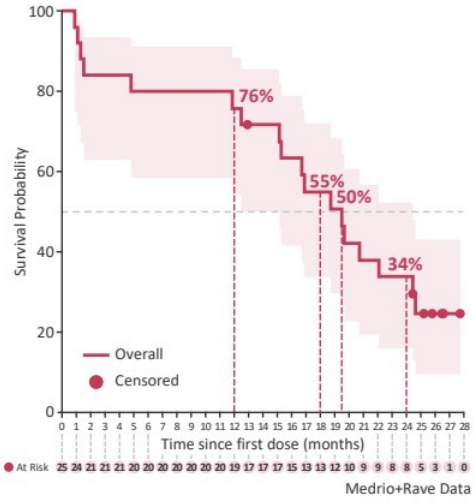
Overall survival

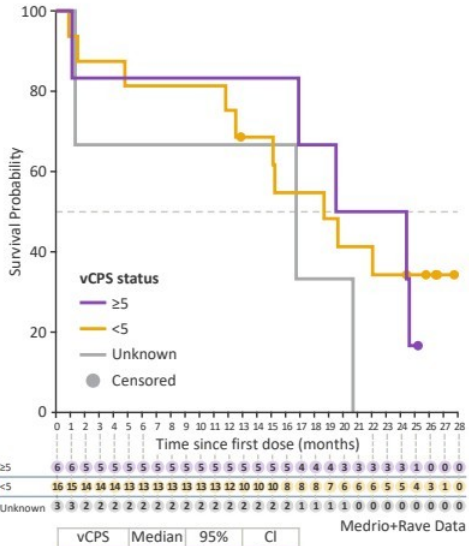
1L GEJ/GC
DKN-01
+ tislelizuma
+ chemothe

Overall Population



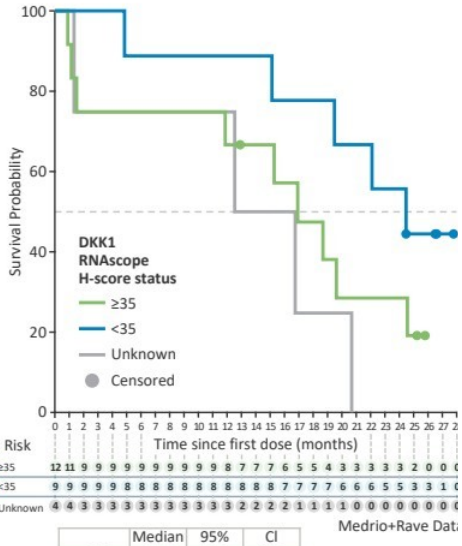
	Median	95%	CI
Overall	19.5	15.2	24.4

By PD-L1 Expression



vCPS	Median	95%	CI
≥5	22.0	1.12	NA
<5	18.7	11.9	NA
Unknown	16.8	1.31	NA

By DKK1 Expression



	Median	95%	CI
≥35	16.9	1.12	NA
<35	24.4	4.83	NA
Unknown	14.6	1.31	NA

DKK1-high: H-score ≥35; | DKK1-low: H-score <35 | PD-L1: Programmed Death-Ligand 1 | vCPS: Visually-Estimated Combined Positive Score

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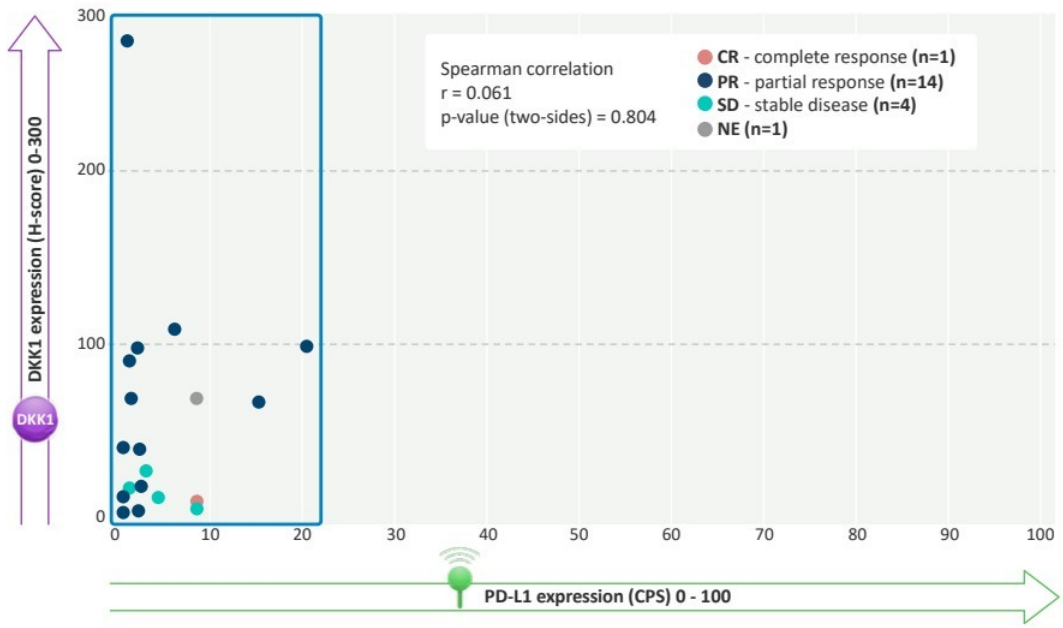
DKK1 and PD-L1 expression are not correlated

1L GEJ/GC
DKN-01
+ tislelizumab
+ chemotherapy



This population had low overall PD-L1 expression

19 As presented at ASCO GI 2022

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Competitive benchmarks for anti-PD-1 + chemotherapy in 1L GEJ/GC patients

1L GEJ/GC
DKN-01
+ tislelizuma
+ chemothe

PD-1 antibodies plus chemotherapy	Nivolumab		Tislelizumab	Pembrolizumab
	Checkmate-649 (All) N=789	Checkmate-649 PD-L1 CPS ≥ 5 N=473	Rationale-305 PD-L1 CPS ≥ 5 N=274	Keynote-859 (All) N=790
OS months (95% CI)	13.7 (12.4, 14.5)	14.4 (13.1, 16.2)	17.2 (13.9, 21.3)	12.9 (11.9, 14.0)
DOR months (95% CI)	8.5 (7.7, 9.9)	9.6 (8.2, 12.4)	9.0 (8.2, 19.4)	8.0
PFS months (95% CI)	7.7 (7.1, 8.6))	8.3 (7.0, 9.3)	7.2 (5.8, 8.4)	6.9 (6.3, 7.2)
ORR (%) (95% CI)	47% (43%, 50%)	50% (46%, 55%)	50.4% (44.3%, 56.4%)	51.3% (47.7%, 54.8%)

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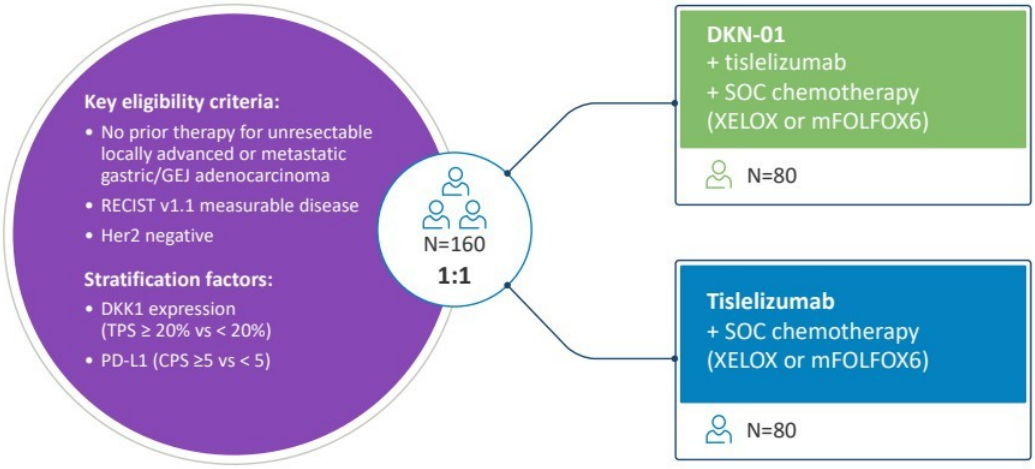
DisTinGuish Part C randomized study

1L GEJ/GC
DKN-01
+ tislelizumab
+ chemotherapy



Primary objective:
PFS DKK1-high

Secondary objectiv
– PFS all patients
– OS, DKK1-high and a
– ORR, DKK1-high and

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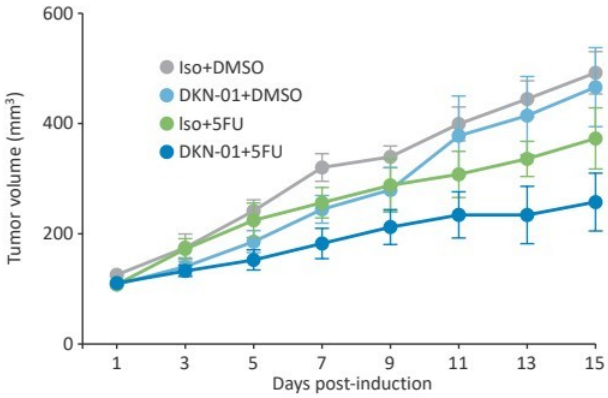
DKN-01

Colorectal cancer development

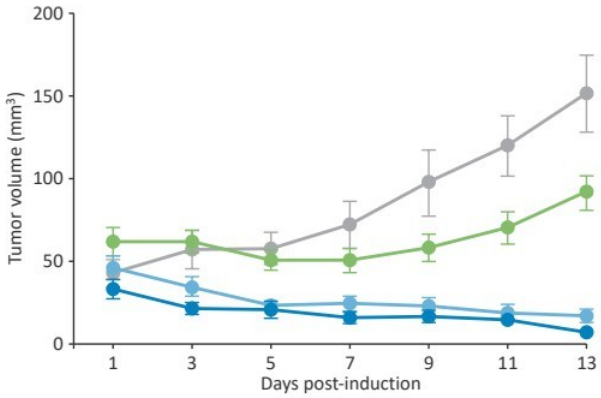
DKN-01 activity in combination with 5-FU chemotherapy in colorectal cancer models

- DKN-01 has efficacy in CRC syngeneic models including SW480
- Additive activity was seen with 5FU chemotherapy
- In a 5FU chemotherapy-resistant model, DKN-01 demonstrates significant inhibition of tumor growth

SW480 parental



SW480 5FU-resistant



Data courtesy of Goel Lab at City of Hope Cancer Center

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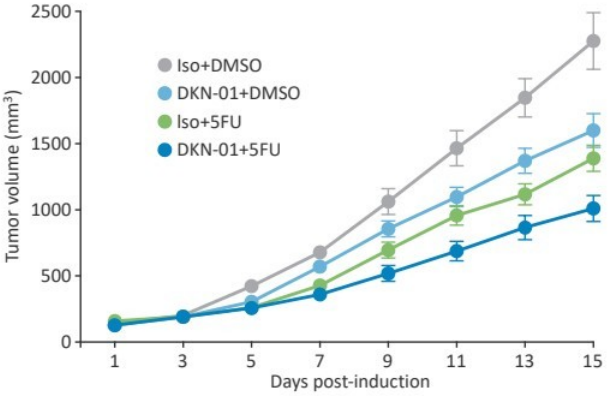
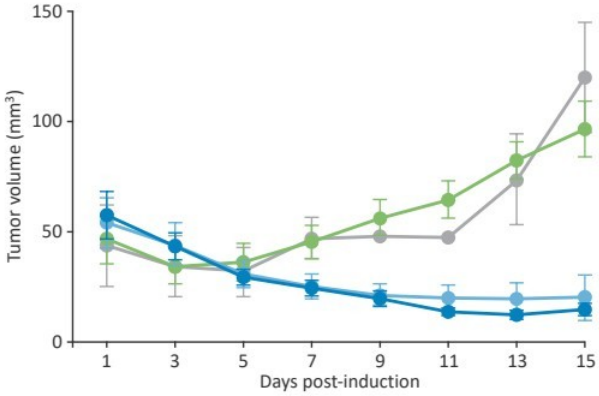
DKN-01 activity in combination with 5-FU chemotherapy in colorectal cancer models

- DKN-01 has efficacy in CRC syngeneic models including HCT116
- Additive activity was seen with 5FU chemotherapy
- In a 5FU chemotherapy-resistant model, DKN-01 demonstrates significant inhibition of tumor growth

HCT116 parental



HCT116 5FU-resistant



Data courtesy of Goel Lab at City of Hope Cancer Center

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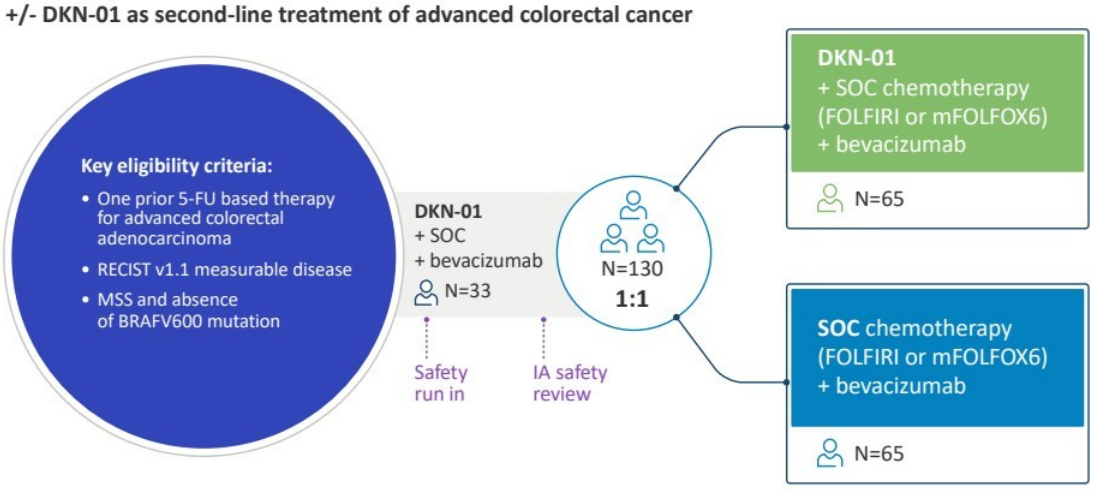
DeFianCe study design: advanced colorectal cancer

2L CRC
DKN-01
+ bevacizumab
+ chemotherapy

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



- **Primary objective:** PFS
- **Secondary objective**
  - ORR
  - DoR
  - OS

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DeFianCe study update – September 13, 2023

2L CRC
DKN-01
+ bevacizun
chemothera

- 33 patients dosed in Part A, completed enrollment in April
- Initial efficacy outcomes drove the decision in late June to open 130 patient randomized controlled Part B
  - Overall response rate > 20%
  - Very high disease control rate
- All of the initial responses were confirmed at their next assessment
- Additional patient responses have occurred since June, with 6 month visits on last patients upcoming
- Full data presentation planned for a medical conference
- Part B enrollment underway with objective of completion in 1 year

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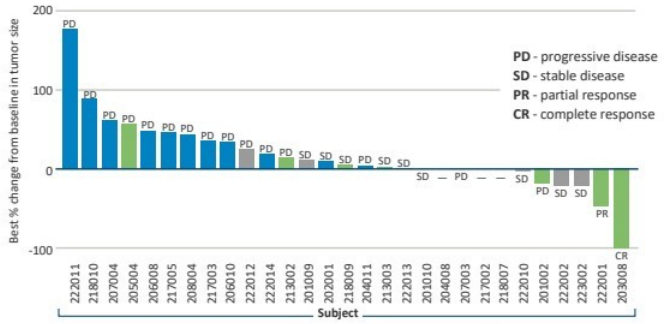
DKN-01

Endometrial cancer development

DKN-01 monotherapy - overall response by DKK1 tumoral expression

Overall response by DKK1 tumoral expression



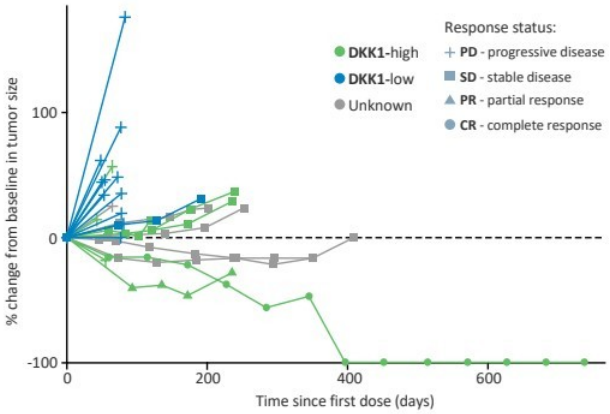
Status	Total	CR	PR	SD	PD	NE	ORR	DCR
DKK1-high (≥18)*	n=8	1	1	3	3	0	25%	63%
DKK1-low (<18)	n=15	0	0	1	11	3	0%	7%
Unknown	n=6	0	0	5	1	0	0%	83%

*H-score ≥ 18, upper tertile of overall study population

DKK1-high tumors have better ORR (25% vs. 0%) and clinical benefit (63% vs. 7%)

Patients with unknown DKK1 expression include 3 patients with durable SD and Wnt activating mutations

Durable clinical benefit in DKK1-high tumors



DKK1-high patients have longer progression-free survival (4.3 vs. 1.8 months [HR 0.26; 95 CI: 0.09, 0.75])

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Complete response in endometrial cancer patient on DKN-01 monotherapy

2L+ EEC
DKN-01
monotherap

Patient:
60 yo female with recurrent endometrial cancer

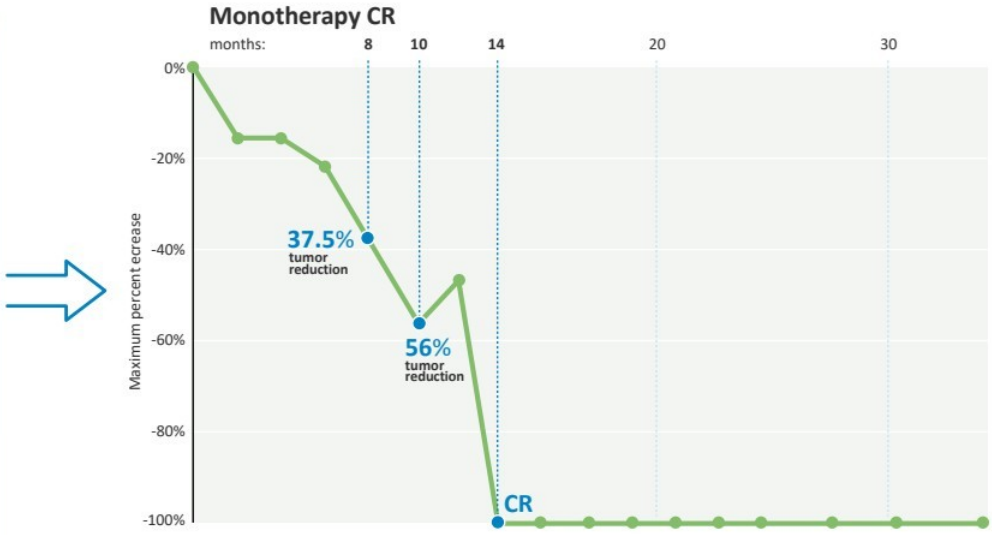
Prior treatment:
radiation and chemotherapy poorly tolerated (neuropathy and thrombocytopenia)

Baseline disease characteristics:
MSI-H, TMB: 46.65

Genetics:
ARID1A, PIK3CA; DKK1-high

Treatment:
DKN-01 monotherapy

Enrolled in July 2018



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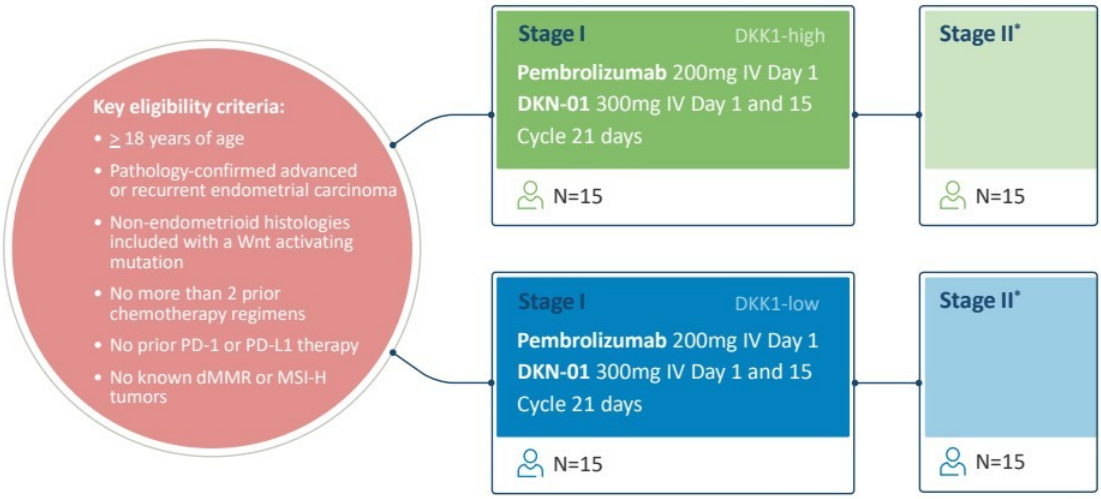
DKN-01 plus pembrolizumab endometrial cancer study

2-3L EEC
DKN-01
+ pembrolizumab



Open-label, phase 2 trial,
Bayesian optimal phase II design,
Investigator-initiated study with pembrolizumab supplied by Merck.

* Move to Stage II based on ORR in Stage I

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center

UAB

Primary objective:
Objective response rate (ORR)

Secondary objectiv
Clinical benefit, PFS, OS, DOR

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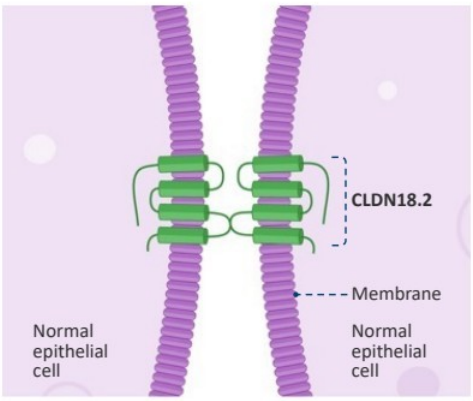
FL-301 (NBL-015)
FL-302 (NBL-016)

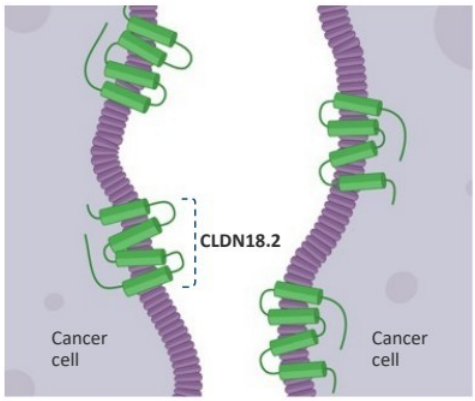
Anti-Claudin18.2 antibodies

The role of Claudin18.2



Normal epithelial cells

- Regulates barrier properties and contributes to cell-to-cell adhesion.
- Expression very limited in normal tissue.
- Typically buried in the tight junction complex of gastric mucosal cells.



Cancer cells

- In cancer, cells lose their polarity and structure.
- CLDN18.2 is overexpressed.
- CLDN18.2 may be exposed and accessible as a target for cancer therapy.

30-40%

of gastric cancer patients have hig Claudin18.2 expression

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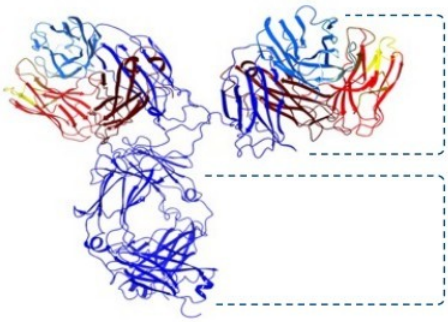
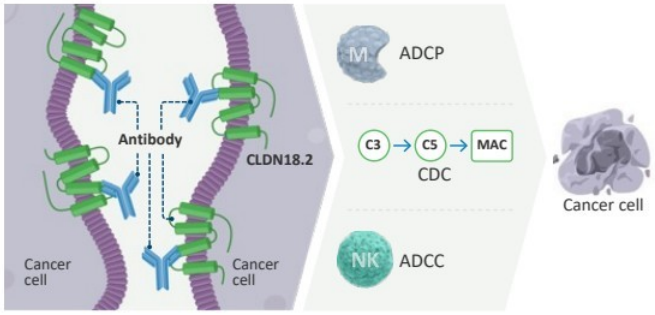
FL-301 (NBL-015) is a potential best-in-class anti-Claudin18.2 antibody with enhanced tumor killing efficacy



- Fully human
- Higher affinity
- Better cell killing

Efficacy could extend to patients with lower CLDN18.2 expression that other currently used anti-CLDN18.2 antibodies.

Anti-CLDN18.2 antibody mechanism



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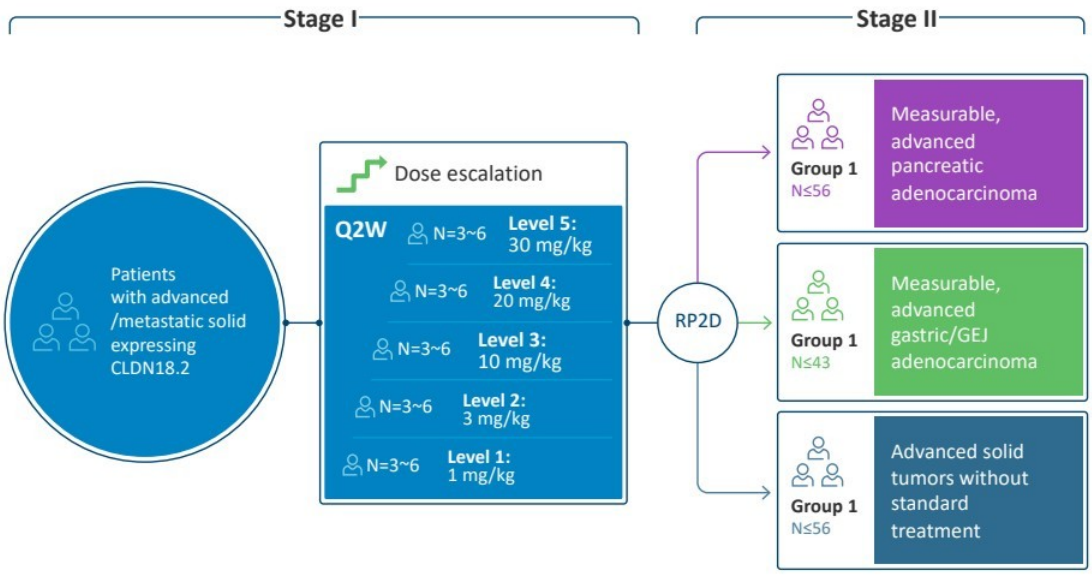
FL-301 (NBL-015) Phase 1 clinical trial being conducted by NovaRock in China

FL-301
CLDN18.2



Evaluation of PK, safety, and activity

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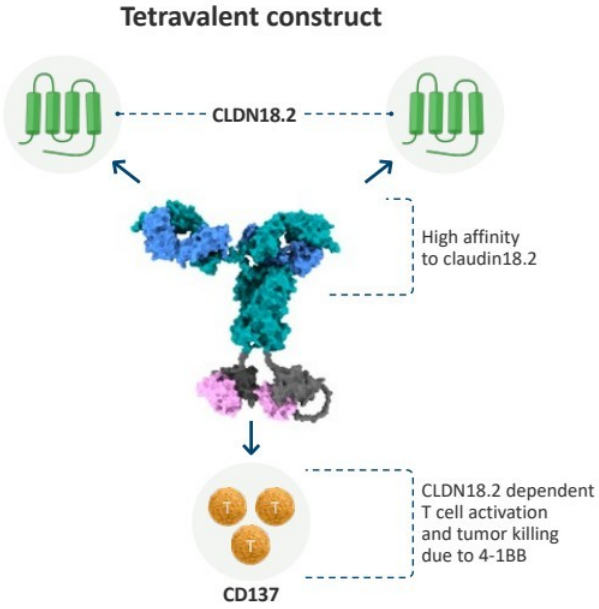
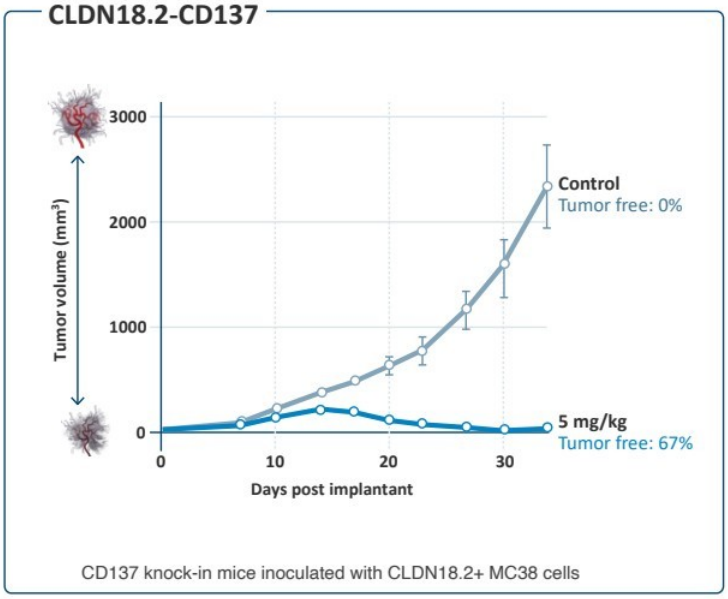
FL-302 (NBL-016) Claudin18.2-CD137 bispecific antibody program





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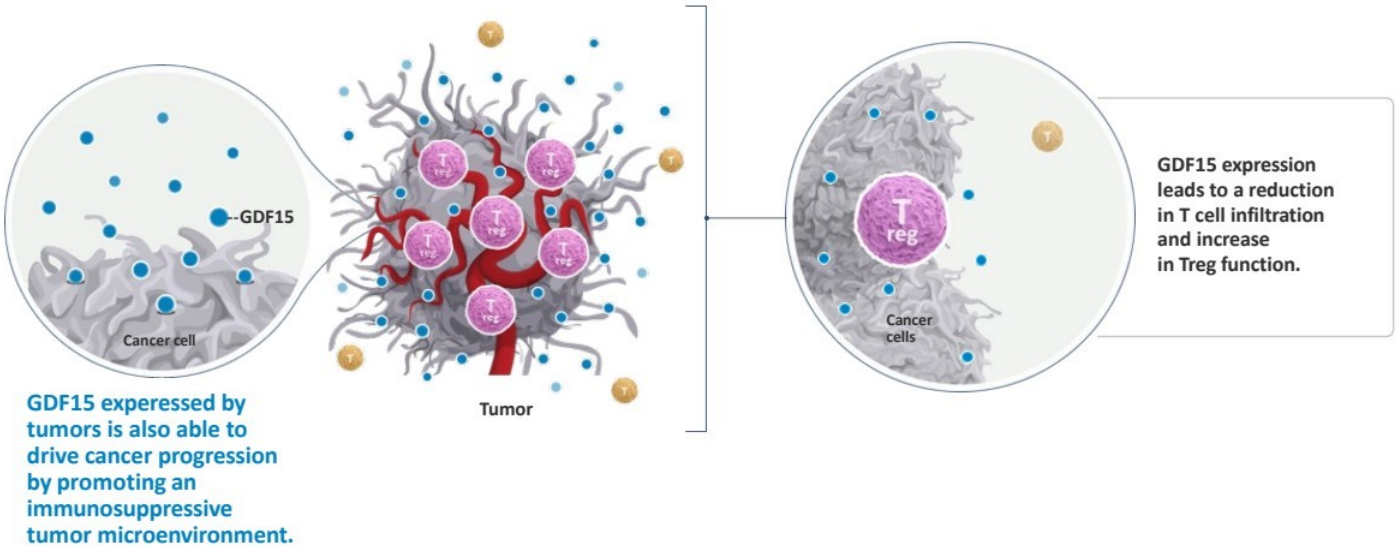
FL-501

Anti-GDF15 monoclonal antibody

The role of GDF15 in cancer



GDF15 experessed by tumors is also able to drive cancer progression by promoting an immunosuppressive tumor microenvironment.

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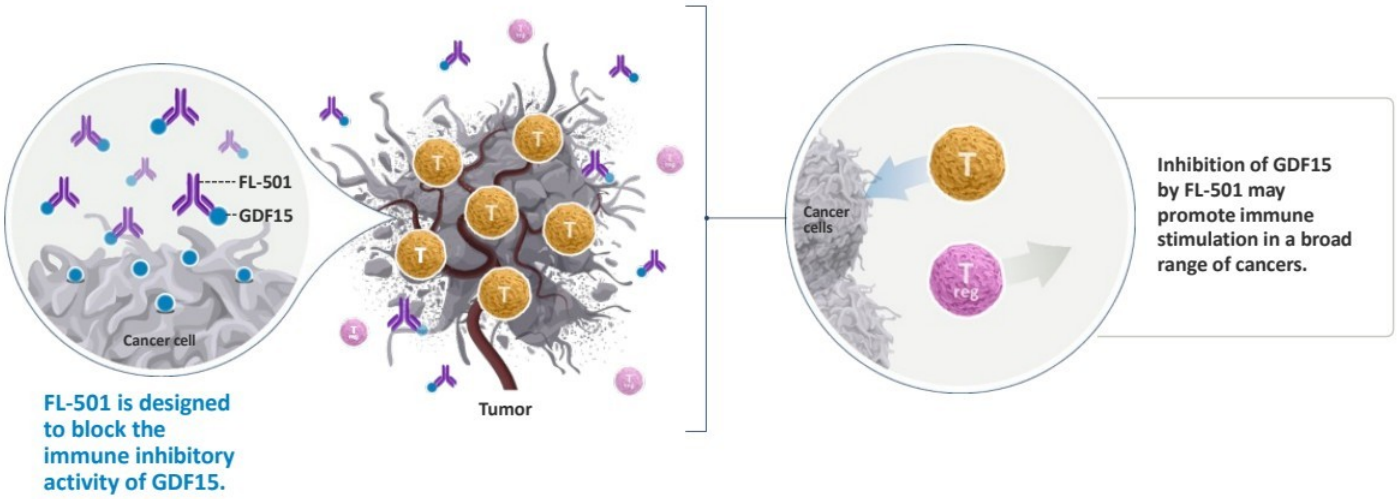
FL-501 mechanism of action



FL-501 is designed to block the immune inhibitory activity of GDF15.

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CORPORATE

Management team

Christopher Mirabelli, PhD
Chairman of the board
LeukoSite · IONIS · HealthCare Ventures

Douglas Onsi
President & chief executive officer
genzyme · HealthCare Ventures · LeukoSite

Gus Lawlor
Chief operating officer
LeukoSite · HealthCare Ventures

Cyndi Sirard, MD
Chief medical officer
SANOFI · genzyme · parexel BIOTECH

Mark O'Mahony
Chief manufacturing officer
TOLERX · MILLENNIUM · LeukoSite

Walter Newman, PhD
Senior research fellow
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NOVARTIS · merrimack

Christine Granfield
Vice president, head of regulatory affairs and quality
NOVARTIS · genzyme

Kevin Lloyd
Vice president, program and alliance management
Ziopharm ONCOLOGY · MILLENNIUM · Biogen

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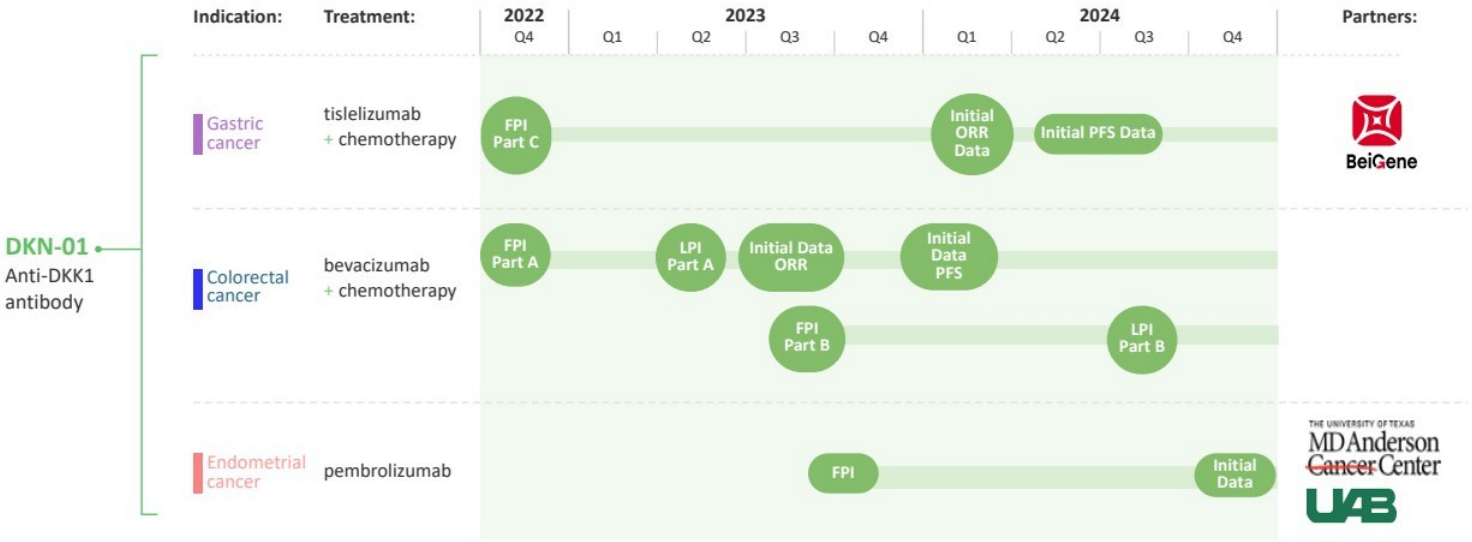
DKN-01 clinical milestones



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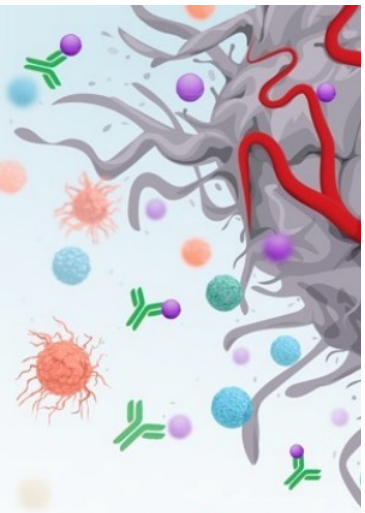
LEAP THERAPEUTICS

company presentation

September 13, 2023



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