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): **July 12, 2022**

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 Global 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 July 12, 2022, Leap Therapeutics, Inc. (the "Company") will host a virtual research and development day (the "R&D Day"). The program will include presentations by members of Leap's leadership team as well external thought leaders in Leap's core development areas. Also on July 12, 2022, the Company issued a press release entitled "Leap Therapeutics Announces Initiation of New DKN-01 Clinical Trials in Gastric Cancer, Colorectal Cancer and Endometrial Cancer." A copy of the corporate presentation for the R&D Day and the full text of the press release are filed as Exhibits 99.1 and 99.2, respectively, to this Current Report on Form 8-K and incorporated herein by reference; provided, however that information on or connected to our website referenced in the Company's press release is expressly not incorporated by reference into or intended to be filed as a part of this Current Report on Form 8-K.

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits.

Exhibit Number	Description
99.1	Leap Corporate Presentation
99.2	Press release dated July 12, 2022
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: July 12, 2022

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

Exhibit 99.1

LEAP THERAPEUTICS
company presentation

DKN-01 R&D Day

July 12, 2022

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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Agenda

DKK1 Biology and DKN-01 Mechanism of action

Gastric cancer:

Samuel Klempner, MD
Massachusetts General Hospital

Colorectal cancer:

Zev Wainberg, MD
UCLA

Endometrial cancer:

Rebecca Arend, MD
University of Alabama at Birmingham

Prostate cancer:

David Wise, MD, PhD
New York University

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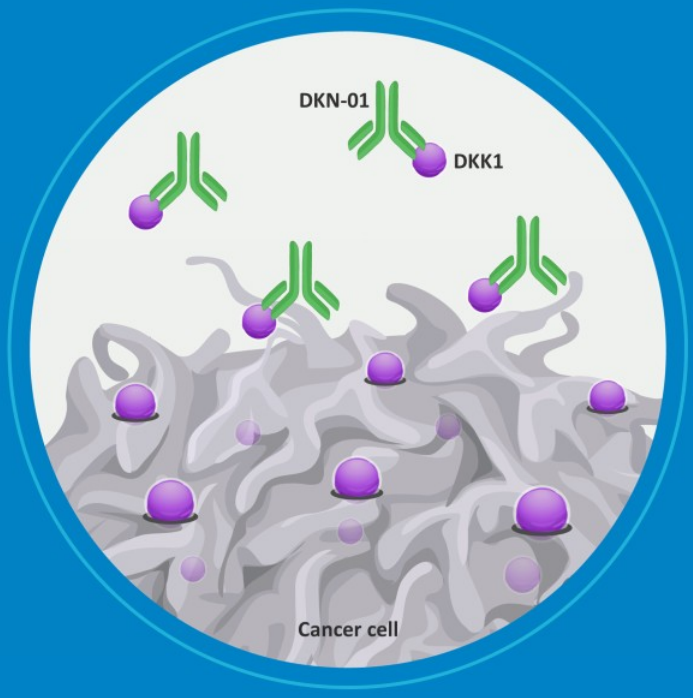
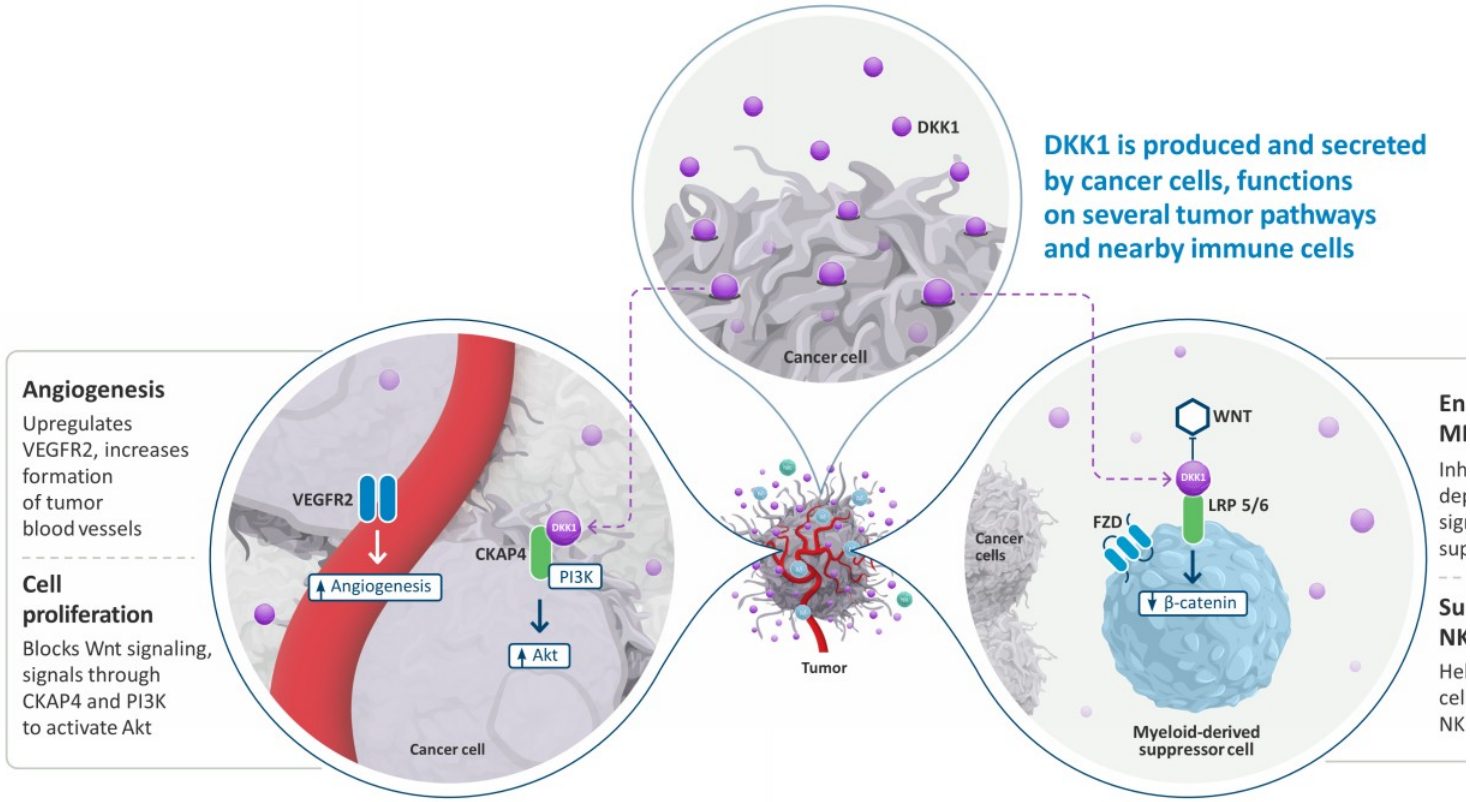
DKN-01 Overview

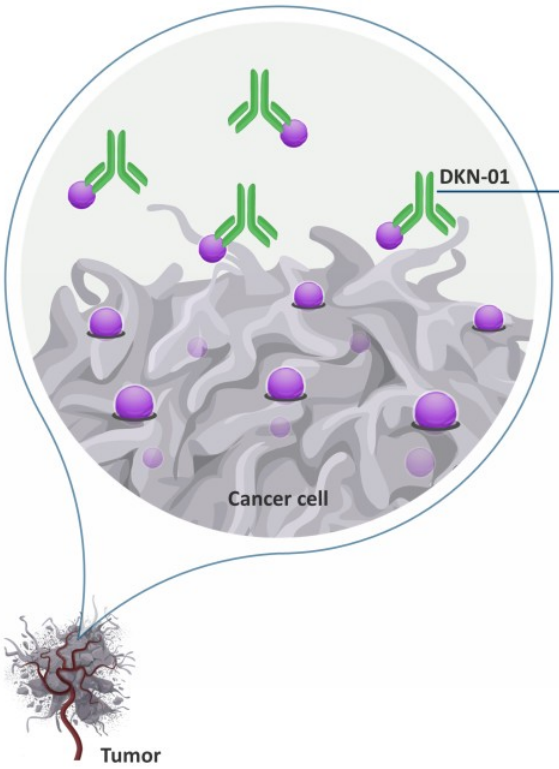


- Biomarker-targeted development
- Single agent activity in three indications
- Combinations with checkpoint inhibitors and chemotherapy
- Strategic partnership with BeiGene
- Important milestones in 2022 and 2023

The role of DKK1 in cancer



DKN-01 - an anti-DKK1 antibody



DKN-01 binds and removes free DKK1 from the TME:

Reduces cell proliferation

Blocks signaling through CKAP4 and PI3K to downregulate akt

Suppress MDSC cel

B-catenin de Wnt signalir MDSCs and immunosup activity

Reduces angiogenesis

Reduces blood vessel formation, upregulates key cytokines, IFNγ, IL-15 and IL-33

Activates NK cells

Upregulates ligands on t production B by activat

Single agent and combination activity demonstrated different tumor types. Well-tolerated as monotherap combination with chemotherapy or checkpoint inhib

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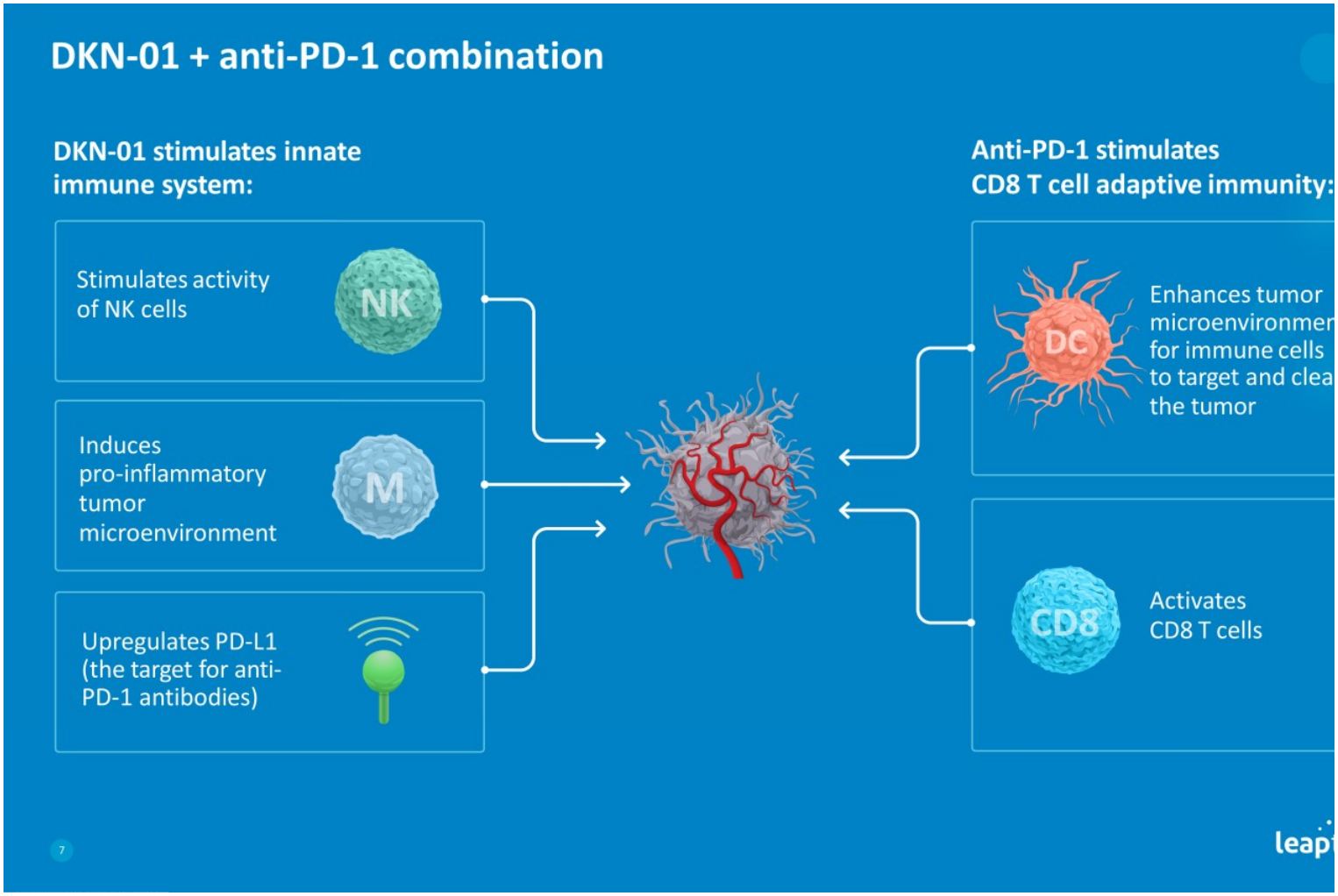
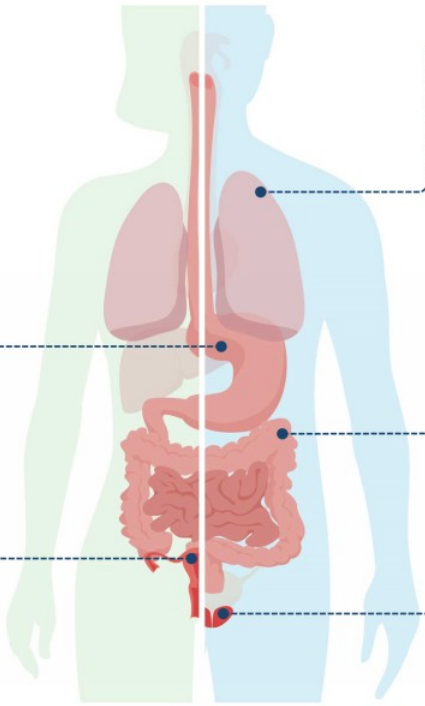
DKN-01 + anti-PD-1 combination



Pipeline



Gastric/GEJ cancer

DKN-01
+ anti-PD-1 tislelizumab
+ chemotherapy (1L)

DKN-01
+ anti-PD-1 tislelizumab (2L)

- 1L PFS data, 2L initial data Q1 2022
- Final 1L data expected in Q3 2022
- 1L Randomized Controlled Trial FPI Q4 2022

Endometrial cancer

DKN-01
+ anti-PD-1 pembrolizumab

- Investigator-initiated study
- FPI Q4 2022

Lung cancer

DKN-01

Colorectal cancer

DKN-01
+ bevacizumab
+ chemotherapy

- FPI Q3 2022

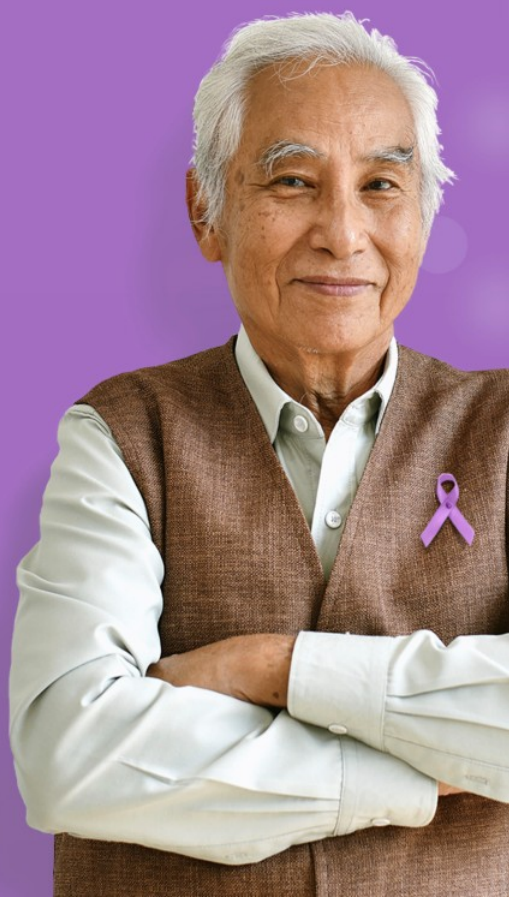
Prostate cancer

DKN-01
+ docetaxel

- Investigator-initiated
- Initial data Q2 2022

DKN-01

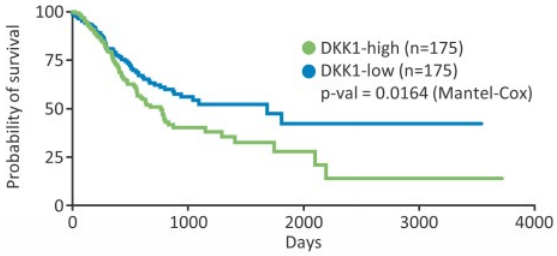
Gastric cancer development



DKK1-high levels are associated with poor survival

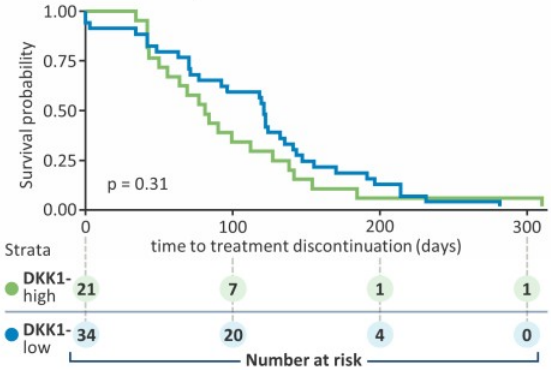
High levels of DKK1 correlate with shorter overall survival In gastric cancer

TCGA STAD dataset

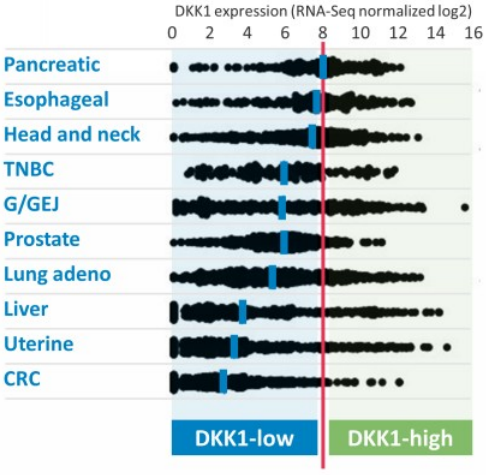


DKK1-high is associated with poor response to first-line platinum + fluoropyrimidine based therapies in GEJ/gastric cancer patients

Collaboration with Tempus



DKK1 expression data (TCGA):

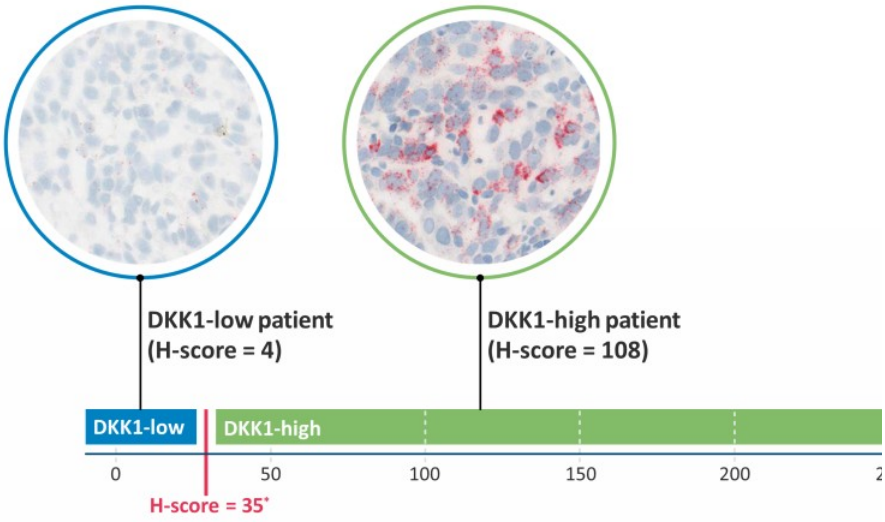


DKK1 expression determined using RNAscope

Chromogenic *in situ* hybridization RNAscope

The biopsy sample is stained to identify DKK1 mRNA

Pathologist determines histology score (H-score), measuring DKK1 expression rather than protein itself



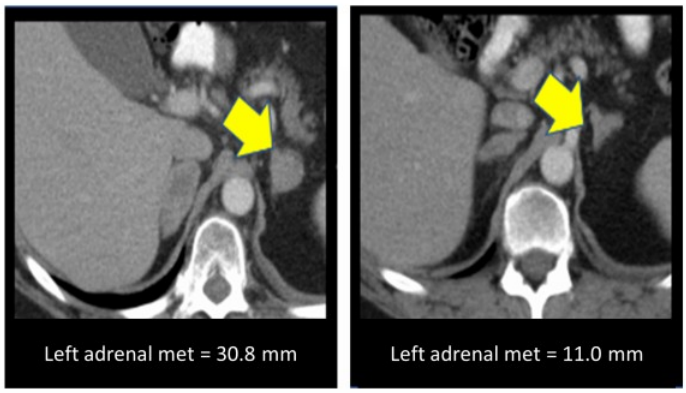
Each red dot is an individual mRNA for DKK1
Number of cells and intensity of staining is converted to H-score

* H-score cut-off at 35 (equating to TPS 20) was identified for gastric cancer from our study of DKN-01 + pembrolizumab

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

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Clinical b

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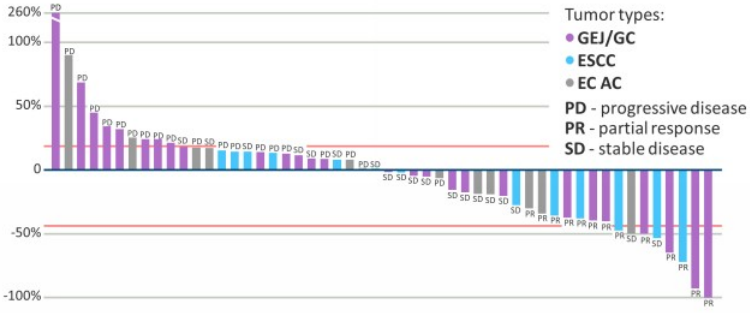
Clinical activity of DKN-01 plus paclitaxel or anti-PD-1 antibody

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)	Ov res rate
DKK1-high	n=11	5.1	7.3	10	5	3	2	1	5 (
DKK1-low	n=20	1.4	4	15	0	3	12	5	0

*DKK1-high ≥ upper tertile (35)

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

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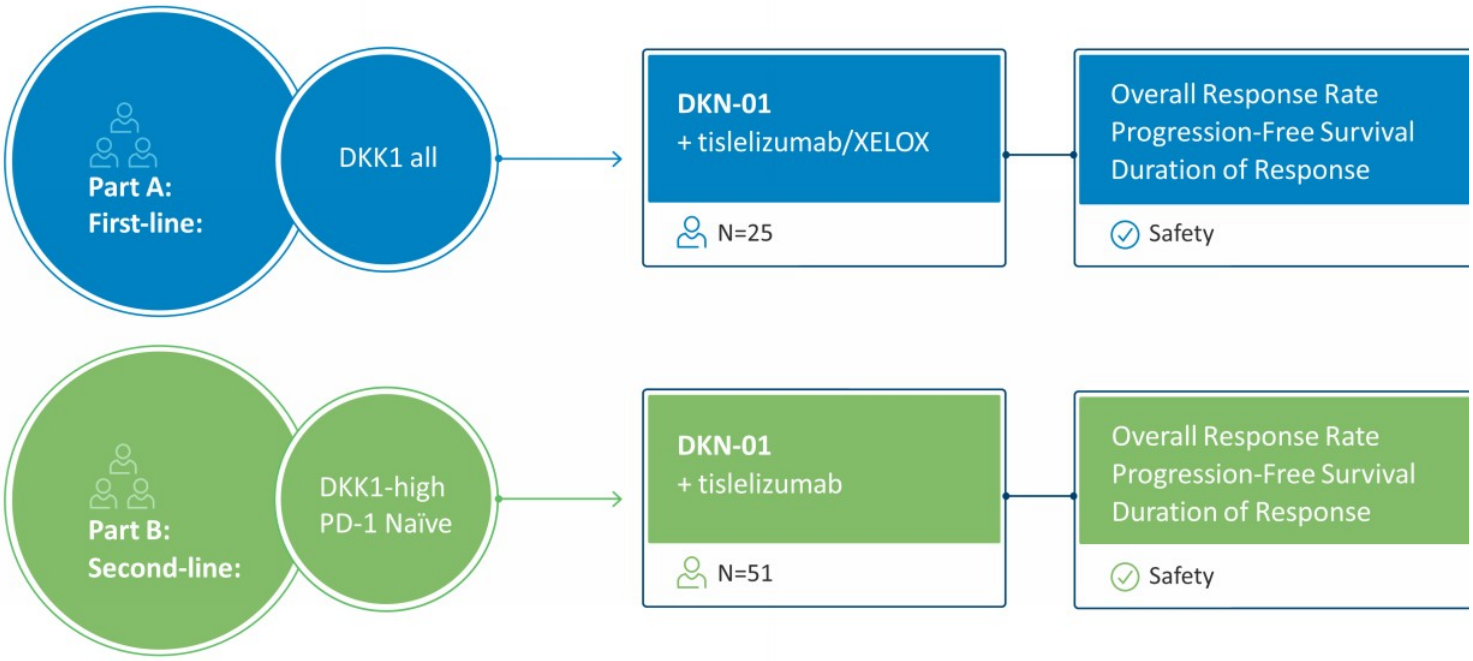
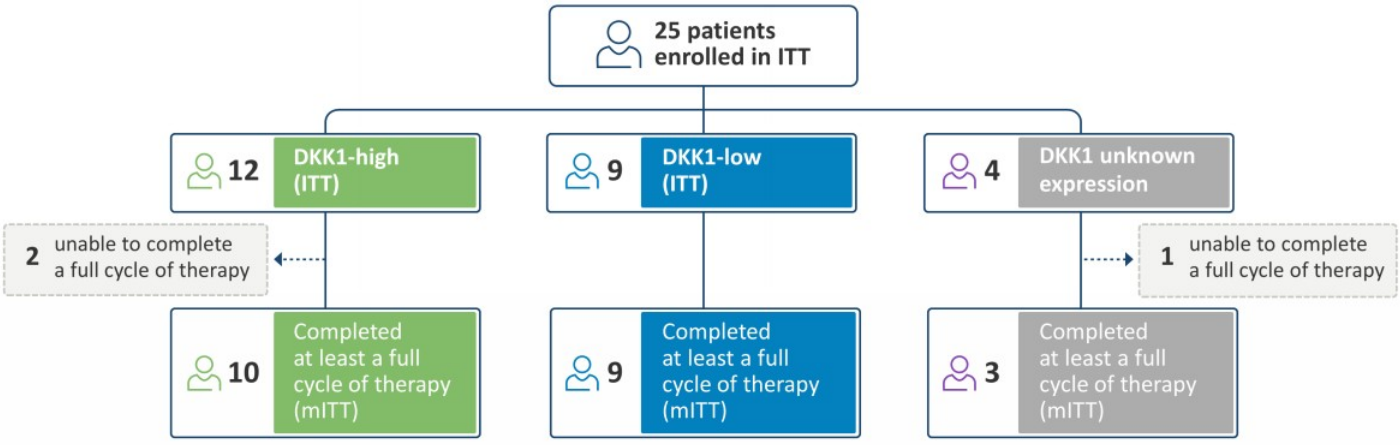
DisTinGuish study design: advanced GEJ/Gastric cancer

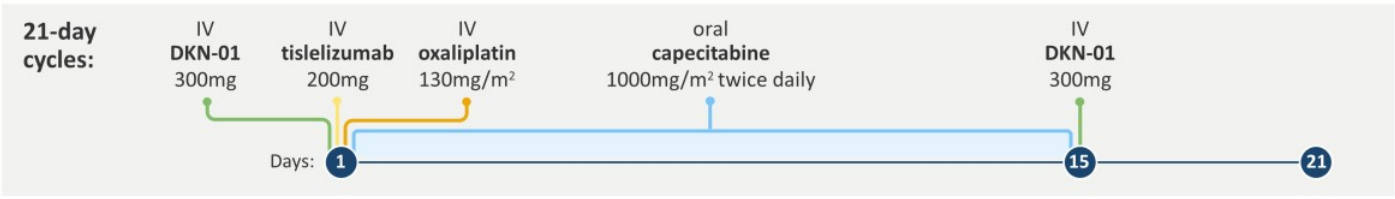
Assess the safety and anti-tumor activity of DKN-01 in combination with tislelizumab +/- chemotherapy



BeiGene | leap

DisTinGuish Part A consort diagram



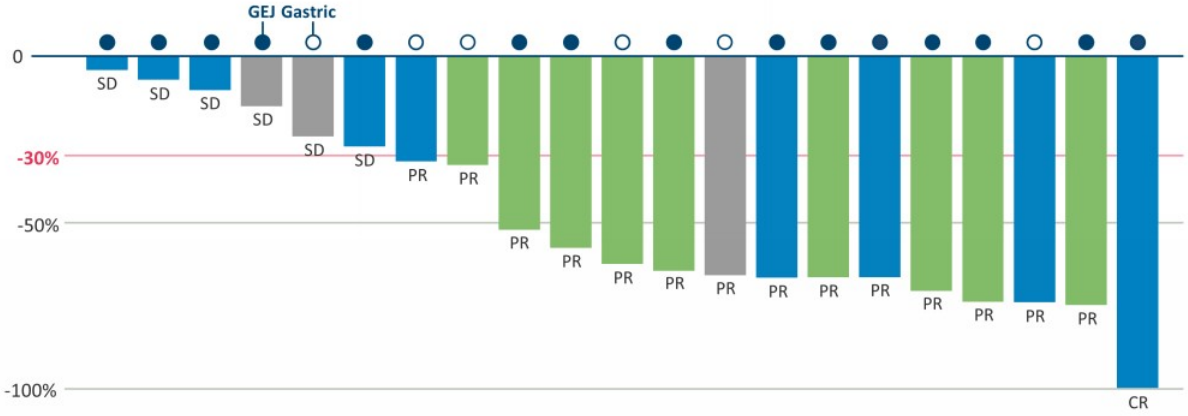


15 DKK1-high: H-score ≥35; DKK1-low: H-score <35

Best overall response by DKK1 expression

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 (4.5%)	0	1 (11.1%)	0
PR - partial response	14 (63.6%)	9 (90.0%)	4 (44.4%)	1 (33.3%)
SD - stable disease	6 (27.3%)	0	4 (44.4%)	2 (66.7%)
PD - progressive disease	0	0	0	0
NE - non-evaluable	1 (4.5%)	1 (10.0%)	0	0

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

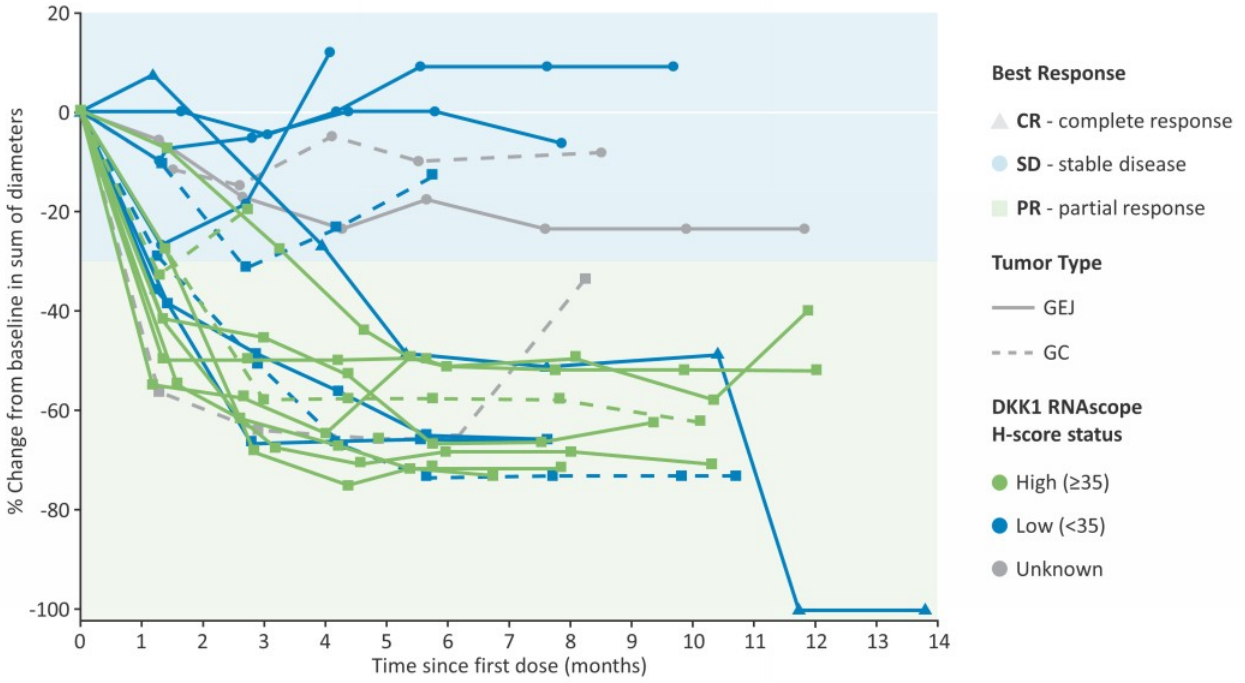
1 PR went to curative surgery with pathological CR

*mITT population includes all patients who received > 1 dose of DKN-01
As presented at ASCO GI 2022

Durable response by DKK1 expression

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

Best % change in sum of diameters

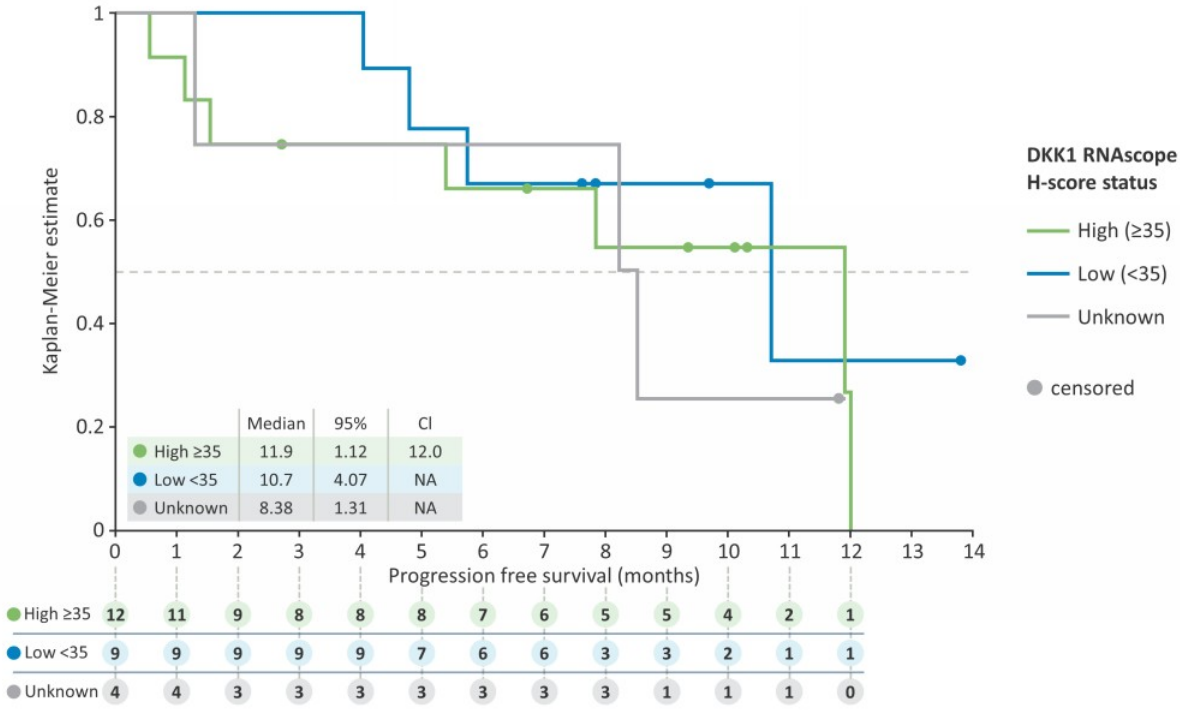


17 As presented at ASCO GI 2022

PFS longer in DKK1-high patients

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

Progression-free survival by DKK1 status (N=25)



	Median	95%	CI
High ≥35	11.9	1.12	12.0
Low <35	10.7	4.07	NA
Unknown	8.38	1.31	NA

High ≥35	12	11	9	8	8	8	7	6	5	5	4	2	1
Low <35	9	9	9	9	9	7	6	6	3	3	2	1	1
Unknown	4	4	3	3	3	3	3	3	3	1	1	1	0

18 As presented at ASCO GI 2022

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for DK
11.9 m

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7.7 m

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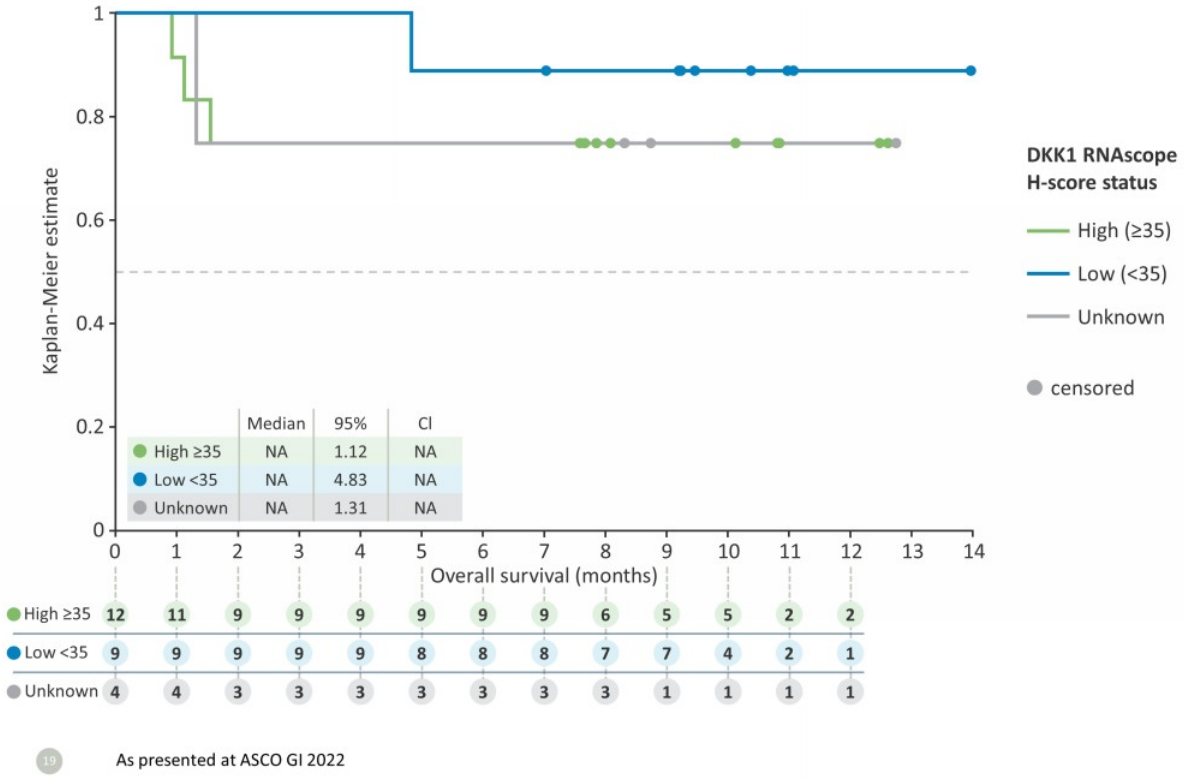
Overall survival not reached

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

Overall survival by DKK1 status (N=25)



	Median	95%	CI
High ≥35	NA	1.12	NA
Low <35	NA	4.83	NA
Unknown	NA	1.31	NA

High ≥35	12	11	9	9	9	9	9	9	6	5	5	2	2
Low <35	9	9	9	9	9	8	8	8	7	7	4	2	1
Unknown	4	4	3	3	3	3	3	3	3	1	1	1	1

19 As presented at ASCO GI 2022

Median
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Best overall response by PD-L1 expression

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

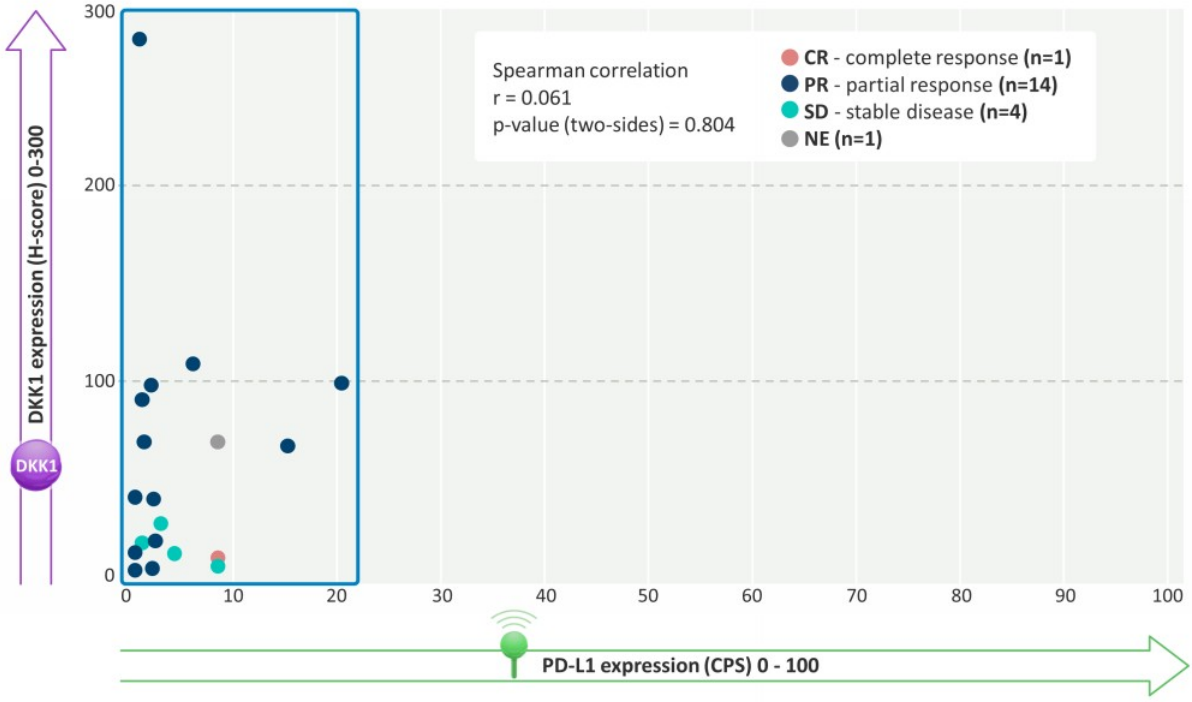
Best % change in sum of diameters

	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%)	4 (57%)*	1 (100%)
SD - stable disease	0	1 (50%)	0	3 (43%)	0
PD - progressive disease	0	0	0	0	0
NE - non-evaluable	1 (25%)	0	0	0	0
	N=6 **67% ORR**		N=14 **79% ORR**		

vCPS: visually-estimated combined positive score; PD-L1: programmed death-ligand 1
*Includes one pathologic CR
As presented at ASCO GI 2022

DKK1 and PD-L1 expression are not correlated

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



21 As presented at ASCO GI 2022

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DKN-01 plus tislelizumab and chemotherapy safety profile

Combination DKN-01+ tislelizumab + capox was well tolerated with manageable toxicity

Most common DKN-01-related adverse events were low grade (G1/2):

Fatigue, nausea, diarrhoea, neutrophil count decreased, platelet count decreased

5 patients experienced six Grade ≥3 DKN-01-related adverse events:

Diarrhoea (1), neutrophil count decreased (1), blood phosphorus decreased (2), pulmonary embolism (2)

No Grade 4 events

TEAEs leading to death (Grade 5) within 30 days of last dose

- Pulmonary embolism (1) assessed by the investigator as related to regimen
- Aspiration pneumonia (1) and hepatic failure (1) both assessed as possibly related to disease progression

Preferred terms:	Part A (No. Pati
TEAEs leading to death within 30 days of last dose	3 (12
Any adverse event	25 (1
Grade ≥ 3 events	14 (5
DKN-01-related	5 (20
Serious adverse events	10 (4
DKN-01-related	2 (8%
Events leading to DKN-01 discontinuation	3 (12
DKN-01-related	1 (4%
Events leading to DKN-01 dose reduction	1 (4%
Drug-related adverse events	
DKN-01-related	14 (5
Tislelizumab-related	17 (6
Capecitabine-related	24 (9
Oxaliplatin-related	25 (1
Regimen-related	25 (1

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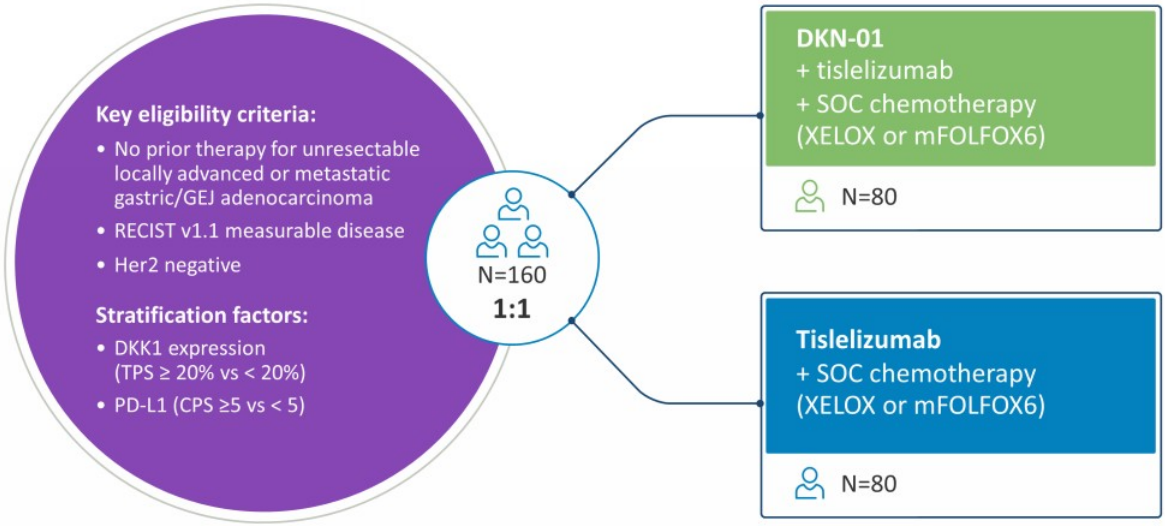
DisTinGuish Part C randomized study

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



DKN-01 highlights in gastric cancer

DKK1 is an important new therapeutic target in gastric cancer

DKK1-high is associated with aggressive biology, poor response to standard 5-FU therapy, and shorter survival

DKN-01
+ anti-PD-1 tislelizumab
+ chemotherapy (1L)

Overall
68% ORR
10.7m PFS

DKK1-high
90% ORR
11.9m PFS

DKK1-low
56% ORR
10.7m PFS

PD-L1 ↓ CPS <5
79% ORR

DKK1-high
PD-L1 ↓ CPS <5
100% ORR

Response is correlated with DKK1 expression and independent of P expression

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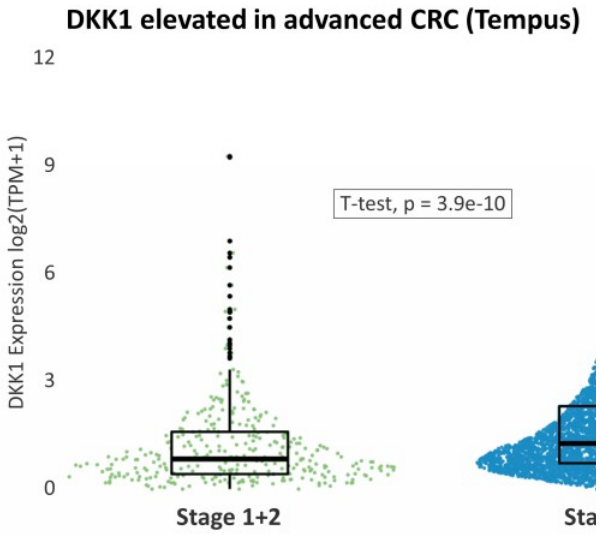
DKN-01

Colorectal cancer development

Rationale for targeting colorectal cancer

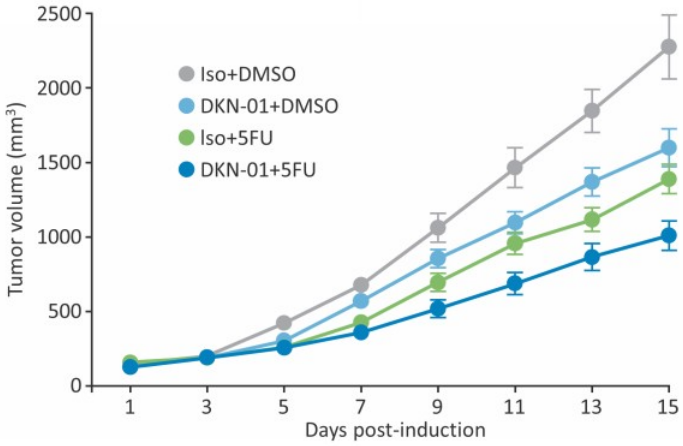
- CRC is characterized by hyperactivation of the Wnt pathway, often believed to be the initiating and driving event
- DKK1 drives resistance to 5FU; DKN-01 has demonstrated prior synergy with 5FU-based regimen in GEA
- Preclinically DKN-01 treatment:
  - Shows additive activity with 5FU and is able to overcome 5FU-resistance in xenograft models
  - Has activity alone and with anti-PD-1 in syngeneic models
  - Has activity in wild type and PIK3CA mutant models alone and with a PIK3CA inhibitor



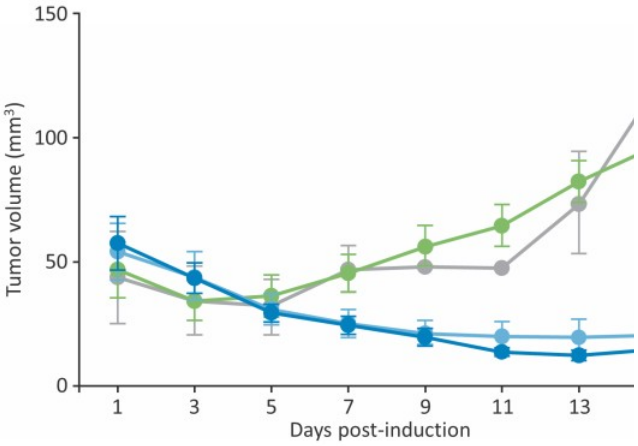
DKN-01 activity in combination with 5-FU chemotherapy in colorectal cance

- 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

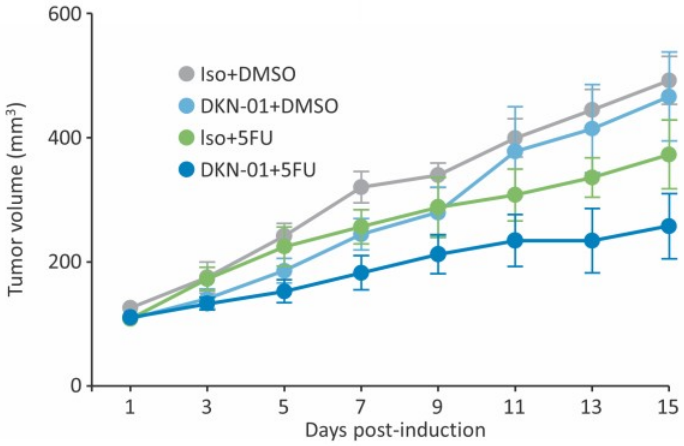


Data courtesy of Goel Lab at City of Hope Cancer Center

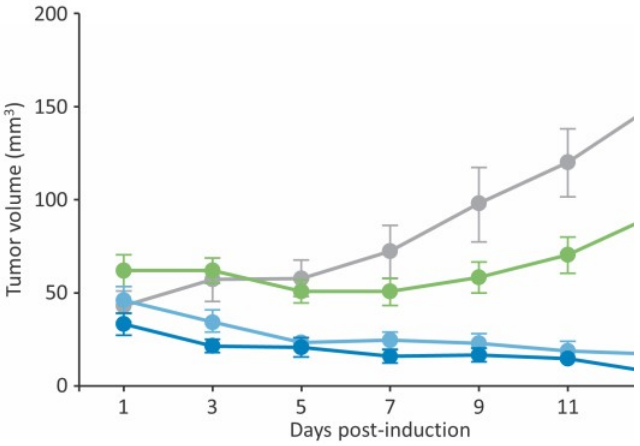
DKN-01 activity in combination with 5-FU chemotherapy in colorectal cance

- 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



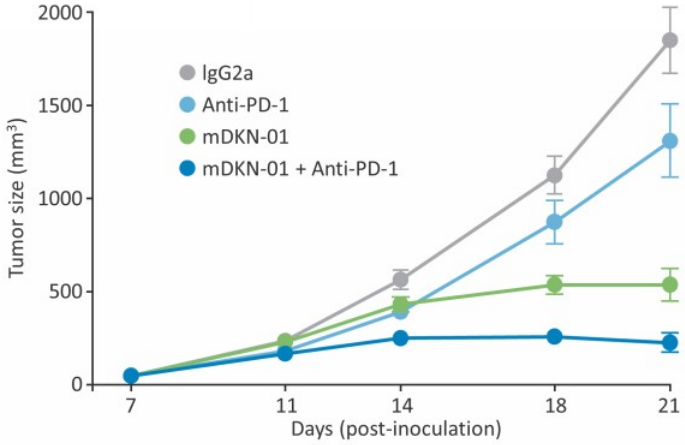
SW480 5FU-resistant



Data courtesy of Goel Lab at City of Hope Cancer Center

DKN-01 activity in combination with PD-1 antibody in colorectal cancer model

- DKN-01 has efficacy in CRC syngeneic models including CT26
- Additive activity was seen with an anti-PD-1 antibody



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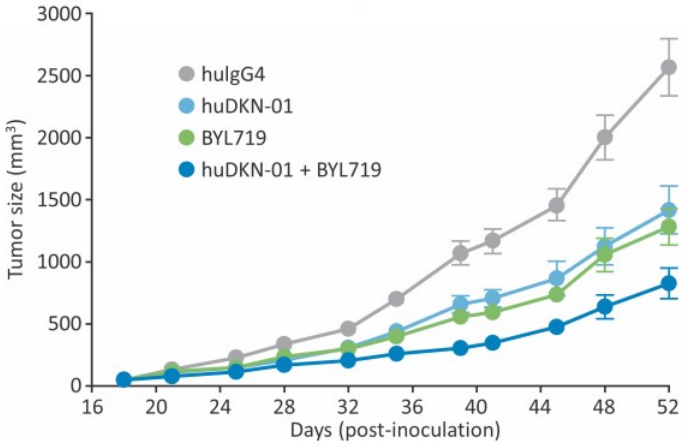
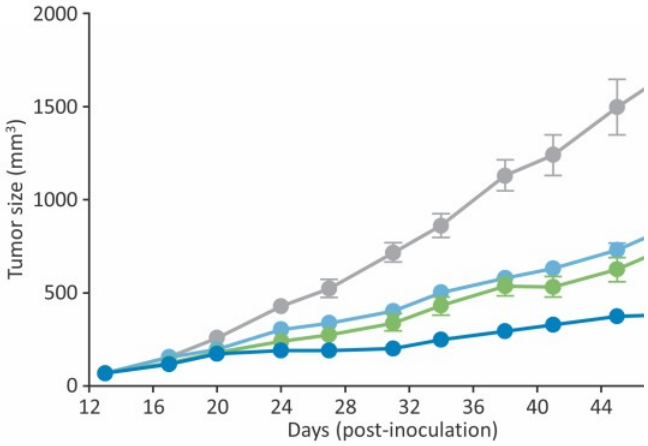
DKN-01 activity in combination with PI3 kinase inhibitor in colorectal cancer

- DKN-01 has efficacy in CRC xenograft models, including with PIK3CA mutation
- Additive activity was seen with an PI3 kinase inhibitor

HCT116 parental



HCT116 + PIK3CA H1047R mutation



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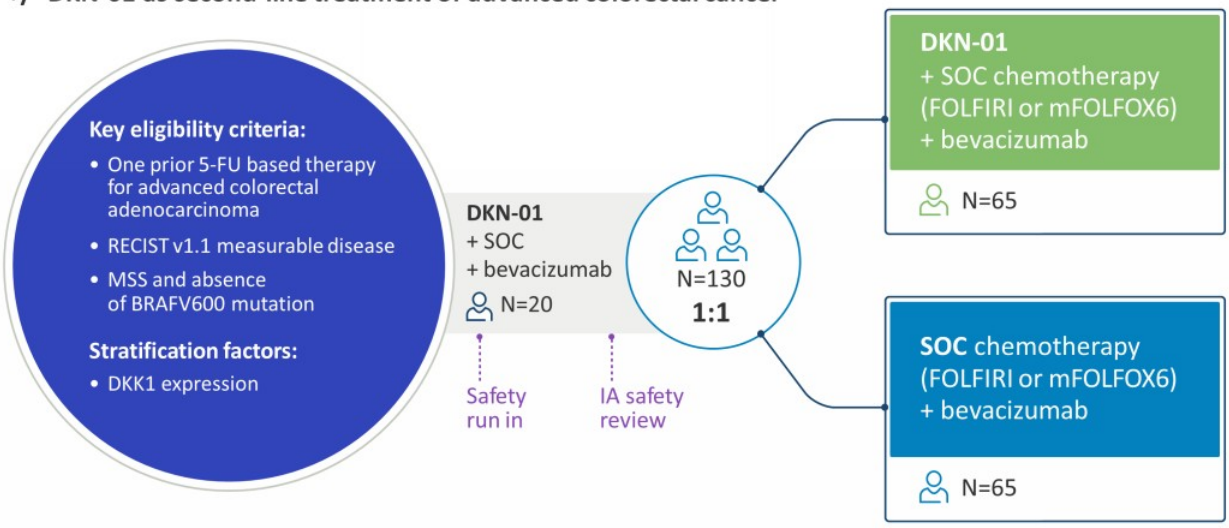
DKN-01 colorectal cancer study

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



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DKN-01

Endometrial cancer development

Endometrial Cancer

5-Year overall and relative survival:

Most common gynecological cancer in the western world

~66,500

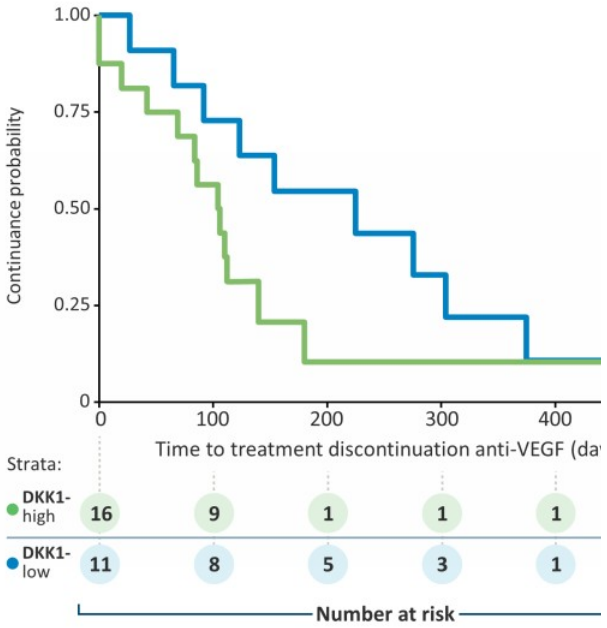
~66,500 annual cases in the United States and the incidence is increasing

Fourth most common cancer in women in the United States

Clinical risk factors include estrogen-only hormone replacement, obesity, chronic anovulation, tamoxifen therapy, nulliparity, early menarche, and late menopause

High DKK1 is associated with poor response to anti-V therapy in endometrioid endometrial cancer patient

Anti-VEGF treatment:



Source: American Cancer Society, Tempus real world evidence

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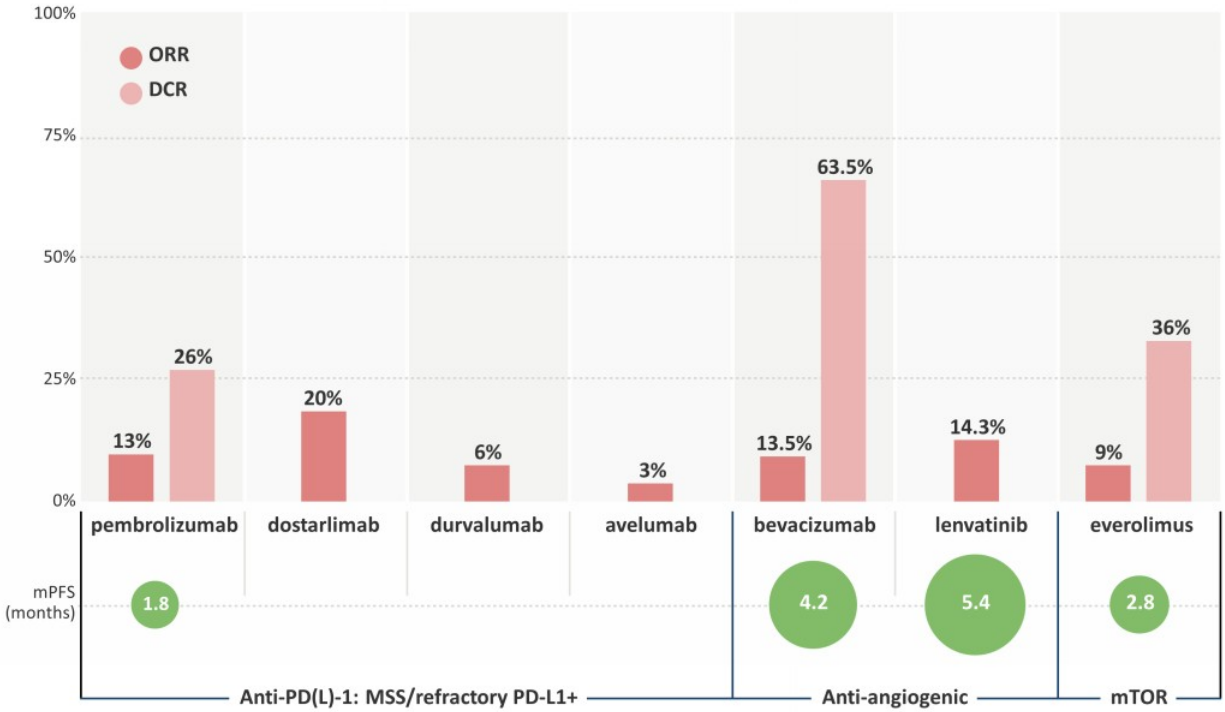
Single agent activity in endometrial cancer



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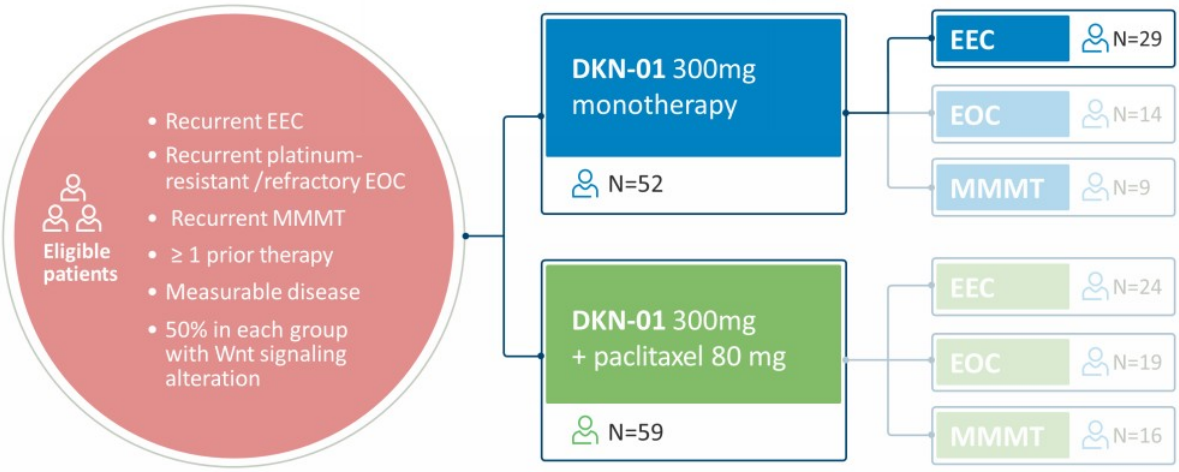
Phase 2 study design evaluating DKN-01 monotherapy and in combination in advanced gynecologic malignancies



EEC - epithelial endometrial cancer
EOC - epithelial ovarian cancer
MMMT - malignant mixed Müllerian cancer

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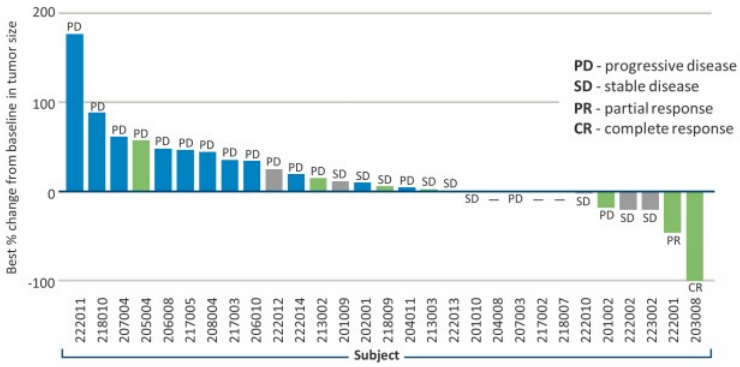
DKN-01 monotherapy - overall response by DKK1 tumoral expression

Overall response by DKK1 tumoral expression



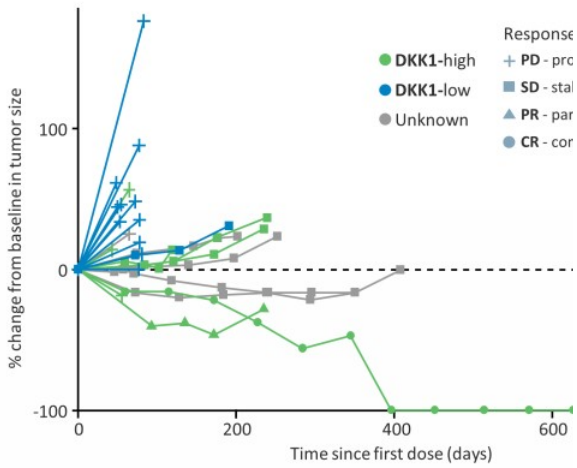
Status	Total	CR	PR	SD	PD	NE	ORR	DCR
DKK1-high (≥18)*	n=8	1	1	3	3	0	25%	63%
DKK1-low (<18)	n=15	0	0	1	11	3	0%	7%
Unknown	n=6	0	0	5	1	0	0%	83%

*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



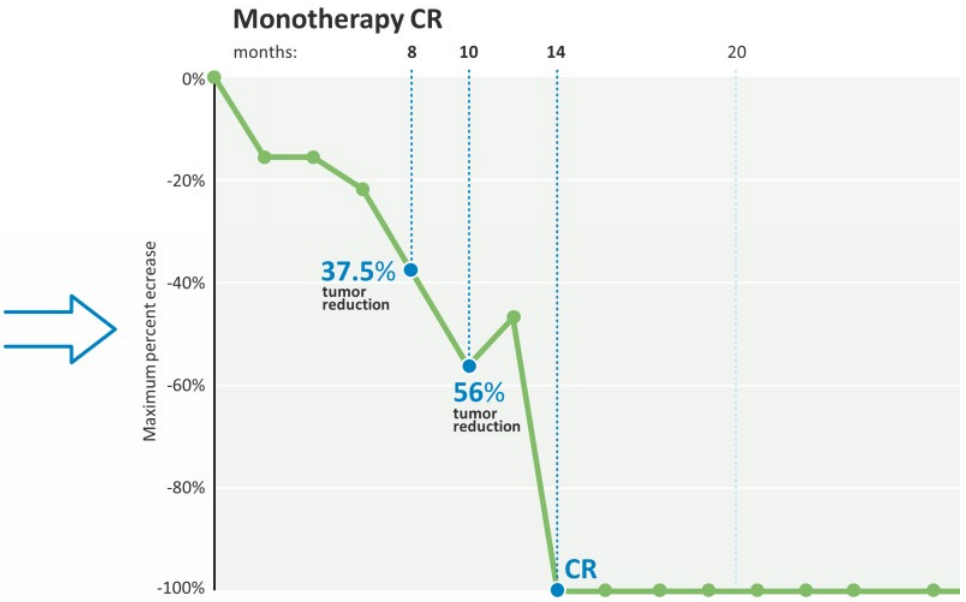
DKK1-high patients have longer progression-free surv (4.3 vs. 1.8 months [HR 0.26; 95 CI: 0.09, 0.75])

Complete response in endometrial cancer patient on DKN-01 monotherapy

- **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

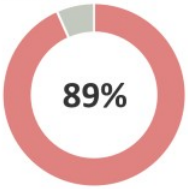
Treatment: **DKN-01** monotherapy

Enrolled in July 2018



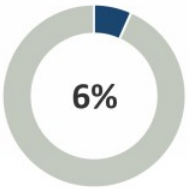
Pembrolizumab + lenvatinib in second-line endometrial cancer

Grade ≥3 treatment-emergent AEs[1]



Any grade treatment-emergent AEs[1]

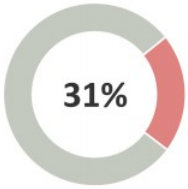
Fatal adverse reactions[1]



most common AE's with Lenvima + Keytruda treated patients:
hypertension (64.0%), hypothyroidism (57.4%), diarrhea (54.2%), nausea (49.5%), decreased appetite (44.8%), vomiting (36.7%), weight decrease (34.0%), fatigue (33.0%), arthralgia (30.5%), proteinuria (28.8%), anemia (26.1%), constipation (25.9%), urinary tract infection (25.6%).

Including gastrointestinal disorders: cardiac disorders: 0.5%, general disorders: 1.5%, infections: 0.7%, decreased appetite: 0.2%, neoplasms, nervous system, psychiatric, renal, reproductive, or respiratory disorders: 0.2% each.

Lenvima discontinuation[1]



Keytruda discontinuation 19%[1,2]**:**
Most common AE's leading to discontinuation of Keytruda: adrenal insufficiency, colitis, pancreatitis and muscular weakness (2% each).

AE's leading to interruption of Keytruda (49%)[2]**:**
fatigue (14%), diarrhea, and decreased appetite (6% e
(5%), renal impairment, vomiting, increased lipase, de
weight (4% each), nausea, increased blood alkaline ph
and skin ulcer (3% each), adrenal insufficiency, increa
hypocalcemia,hypomagnesemia, hyponatremia, peri
edema, musculoskeletal pain, and syncope (2% each)

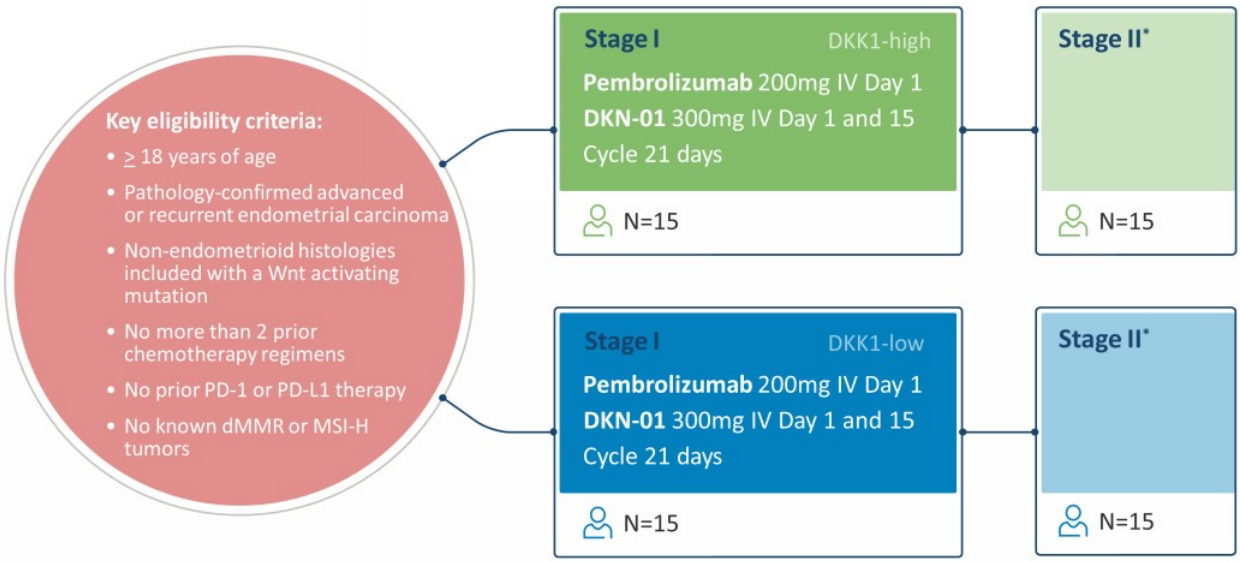
AE's leading to reduction or interruption of Lenvima
fatigue (32%), hypertension (26%), diarrhea (18%), nausea, palmar-plantar erythrodysesthesia, vomiting decreased appetite (12%), musculoskeletal pain (11% stomatisis (9%), abdominal pain, herorrhades (7% eac renal impairment, decreased weight (6% each), rash, headache, increased lipase, and proteinuria (5%

	Population:	n	ORR	CR	PR
Lenvima + Keytruda KN-775	**Post platinum-based therapy, all-comers (dMMR + pMMR)**	**411**	**31.9%**	**6.6%**	**25.3%**
	Post platinum-based therapy pMMR	**346**	**30.3%**	**5.2%**	**25.1%**

[1]KEYNOTE-775 data presented at SGO 2021
[2]FDA Approves LENVIMA® (lenvatinib) plus KEYTRUDA® (pembrolizumab) Combination Treatment for Patients with Certain Types of Endometrial Carcinoma. *https://www.eisai.com/news/2019/news201967.html*

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.

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center

UAB

* Move to Stage II based on ORR in Stage I

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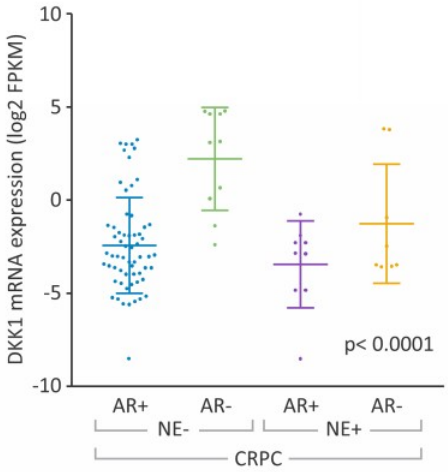
DKN-01

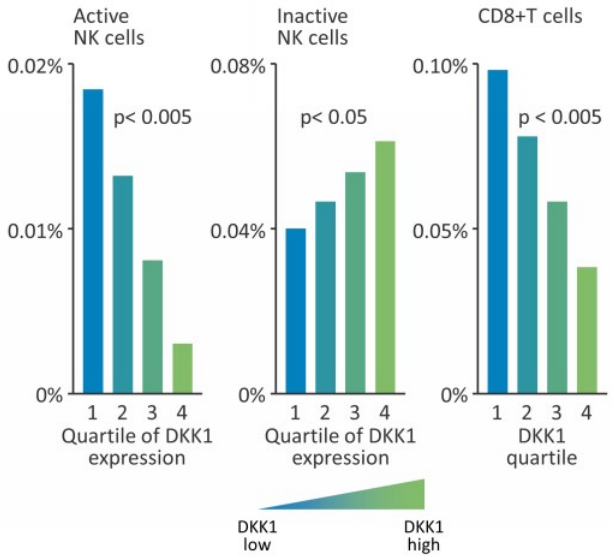
Prostate cancer development

DKK1 and DKN-01 in prostate cancer

DKK1 expression is regulated by AR in CRPC tumor biopsies



CIBERSORT analysis shows DKK1 expression associated with reduced inflammatory infiltrate



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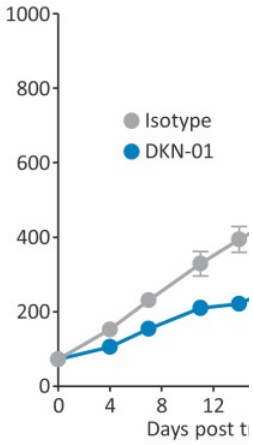

David Wise ASCO 2017

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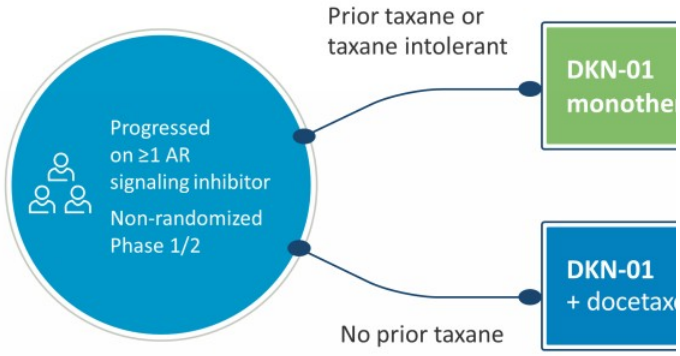
Investigator-initiated study in advanced metastatic castration-resistant prostate cancer (mCRPC)

DKK1 is upregulated in prostate cancers with low Androgen Receptor (AR) expression.

DKN-01 delays prostate cancer growth in pre-clinical models in an NK-cell dependent manner.



Investigator-initiated study in advanced metastatic castration-resistant prostate cancer (mCRPC)

2L+ mCRPC
DKN-01
+ docetaxel

Baseline characteristics:

DKN-01 + Docetaxel	300mg N/A N=4	600mg N/A N=3	300mg 75mg/m² N=3	600mg 75mg/m² N=3
Age	64.5	74	66	68
Adenocarcinoma, n (%)	4 (100%)	3 (100%)	3 (100%)	1 (33%)
Neuroendocrine carcinoma, n (%)	0	0	0	2 (67%)
Aggressive variant (AVPC), n (%)	1 (25%)	0	1 (25%)	3 (100%)
APC mutation, n (%)	1 (25%)	1 (33%)	1 (33%)	0
CTNNB1 mutation, n (%)	0	2 (67%)	0	0

Safety data overview:

- No DKN-01 related Grade ≥ 3 adverse events occurred in either cohort
- No unexpected docetaxel-related Grade ≥ 3 AEs were observed

DKK1 expression in 42% of samples tested:

DKK1 expression	N=24
H-score 0	15 (58.3%)
H-score ≥1	10 (41.7%)
H-score ≥10	5 (20.8%)
H-score ≥35	3 (12.5%)

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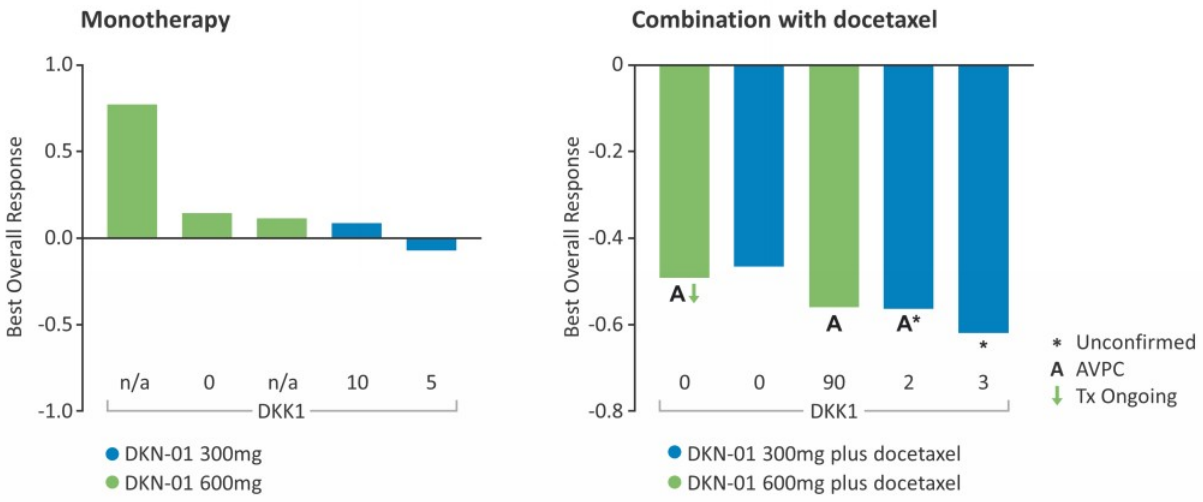
DKN-01 activity in advanced mCRPC patients

2L+ mCRPC
DKN-01
+ docetaxel



	Monotherapy N=7	Combination N=6
PR - partial response	0	5 (83.3%)
SD - stable disease	2 (28.6%)	0
PD - progressive disease	3 (42.9%)	0
NE - non-evaluable	2 (28.6%)*	1 (16.7%)*

1 NE patient in each group had no measurable disease at baseline

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DKN-01 activity in combination with docetaxel

2L+ mCRPC
DKN-01
+ docetaxel

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docetaxe
34% PSA50

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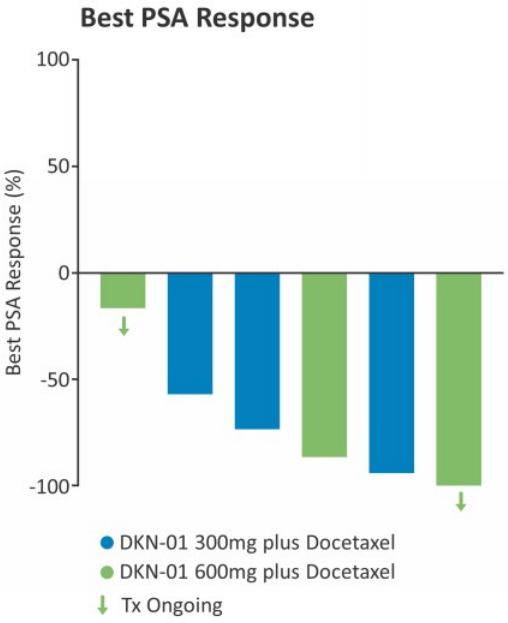

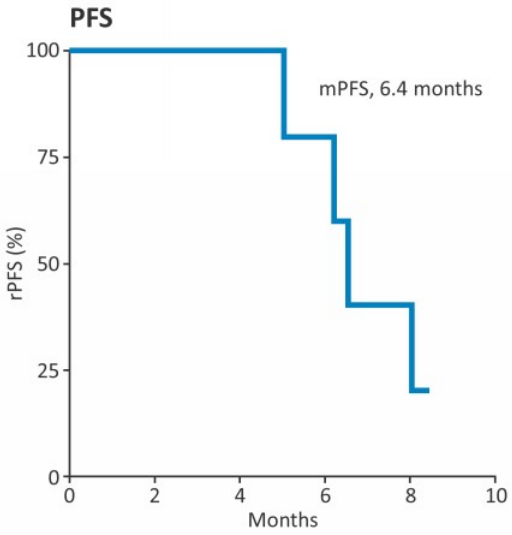

rPFS (n=6) pts treated with DKN-01 plus Docetaxel.

Confirmed partial response with deepening of response on monotherapy

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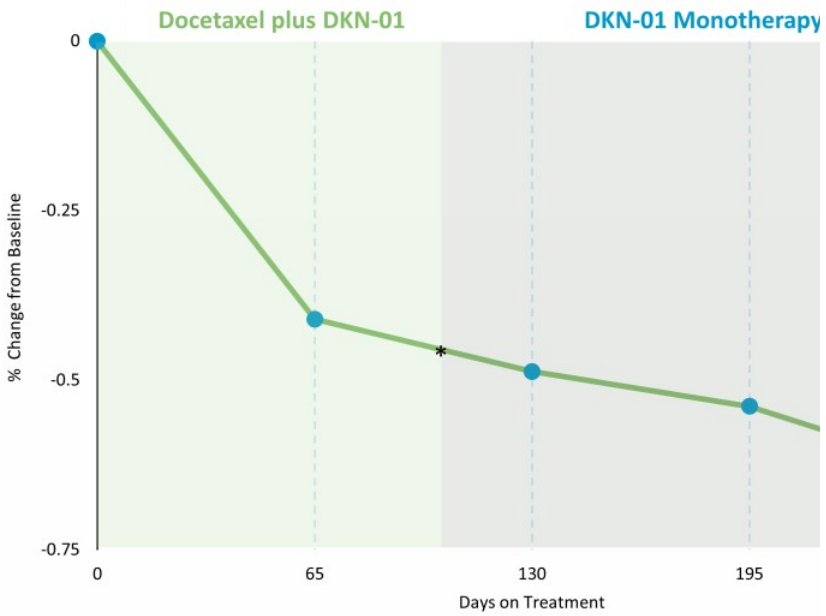
Patient:
69 yo male with metastatic castration resistant prostate cancer

Prior treatment:
Radical prostatectomy, pelvic RT, enzalutamide + 6 cycles of prostvac, bicalutamide, Lupron with immediate progression, darolutamide, sipuleucel-T with new liver lesions and biopsy proven prostate adenocarcinoma

Biomarkers:
NHTL1 mutation, DKK1 H-score = 0

Treatment:
DKN-01 plus docetaxel transitioned to DKN-01 monotherapy



Continued tumor regression with DKN-01 treatment observed after discontinuation of docetaxel

* Docetaxel discontinued due to toxicity

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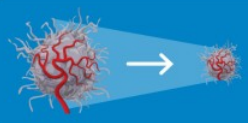
DKN-01 highlights in prostate cancer

Non-clinical studies identified DKK1 as being upregulated in prostate cancers with low Androgen Receptor expression and that inhibition of DKK1 delayed prostate cancer growth

DKN-01 in combination with docetaxel showed promising clinical responses in unselected patients by both RECIST and PSA50 criteria



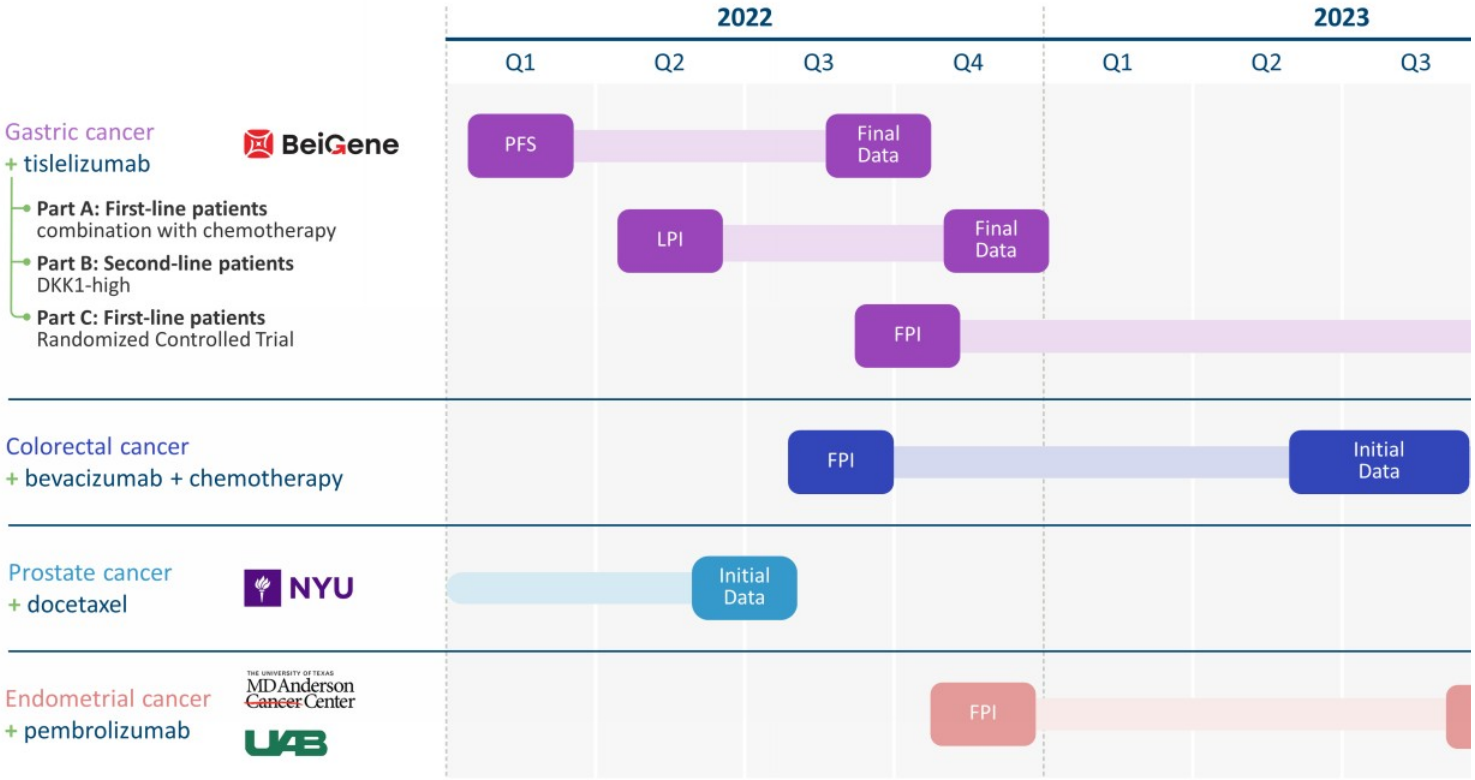
Clinical activity was particularly promising in patients with Aggressive Variant Prostate Cancer

Retrospective correlation of anti-tumor activity with biomarker status is ongoing

DKN-01 DEVELOPMENT STRATEGY

2022-2023 Milestones

Leap 2022-2023 clinical milestones



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QUESTIONS & ANSWERS

Leap Therapeutics Announces Initiation of New DKN-01 Clinical Trials in Gastric Cancer, Colorectal Cancer and Endometrial Cancer

Randomized Controlled First-Line Gastric Cancer Trial of DKN-01 plus tislelizumab and chemotherapy in collaboration with BeiGene

Leap to host R&D Day today at 12:00 p.m. ET

CAMBRIDGE, Mass., July 12, 2022 – Leap Therapeutics, Inc. (Nasdaq:LPTX), a biotechnology company focused on developing targeted and immuno-oncology therapeutics, and BeiGene, Ltd. (Nasdaq: BGNE; HKEX: 06160; SSE: 688235), a global, science-driven biotechnology company focused on developing innovative and affordable medicines to improve treatment outcomes and access for patients worldwide, today announced the initiation of Part C of the ongoing DisTinGuish study to evaluate DKN-01, Leap's anti-Dickkopf 1 (DKK1) antibody, in combination with tislelizumab, BeiGene's anti-PD-1 antibody, and chemotherapy compared to a tislelizumab and chemotherapy control arm, in patients with gastric or gastroesophageal junction cancer (G/GEJ).

Additionally, Leap is initiating a new company-sponsored trial of DKN-01 in combination with standard of care bevacizumab and chemotherapy in second-line patients with colorectal cancer that is designed to expand into a randomized study. Leap is also supporting an investigator-initiated trial of DKN-01 plus pembrolizumab in patients with endometrial cancer to be conducted at The University of Texas M.D. Anderson Cancer Center and at the University of Alabama at Birmingham.

Leap's management team, together with key opinion leaders, will host an R&D Day today to provide updates on the Company's DKN-01 program including G/GEJ, colorectal cancer, endometrial cancer, and prostate cancer.

"Since the presentation of the data for DKN-01 plus tislelizumab and chemotherapy in first-line G/GEJ patients demonstrating compelling overall response rates and progression-free survival, Leap and BeiGene have been working together to create an optimal global strategy for this unique combination therapy. We are excited to enhance the development program and our collaboration with BeiGene through a randomized controlled trial in first-line patients, with a focus on those patients whose tumors express high levels of DKK1," said Douglas E. Onsi, President and Chief Executive Officer of Leap.

"Based on our clinical and preclinical data, Leap is committed to developing DKN-01 aggressively in multiple indications," said Cynthia Sirard, MD, Chief Medical Officer of Leap. "Through a strategic review and prioritization process, we have decided to initiate a company-sponsored study in second-line colorectal cancer patients of DKN-01 in combination with standard of care bevacizumab and chemotherapy. We will also support an investigator-initiated study in endometrial cancer patients of DKN-01 in combination with pembrolizumab, building on previous data showing single-agent activity of DKN-01."

R&D Day:

Leap's management team will host an R&D Day today at 12:00 p.m. Eastern Time and will be joined by key opinion leaders:

Samuel Klempner, MD, Associate Professor at Harvard and Massachusetts General Hospital;

Zev Wainberg, MD, Co-Director of the GI Oncology Program at University of California Los Angeles;

Rebecca Arend, MD, Assistant Professor at University of Alabama at Birmingham Comprehensive Cancer Center; and

David Wise, MD, PhD, Assistant Professor at NYU Langone Health.

The live webcast presentation of the R&D Day can be accessed by registering at https://edge.media-server.com/mmc/p/4zp7m6pw. A replay of the event will be available for a limited time and may be accessed on the Investors page of the Company's website at https://investors.leaptx.com/

Gastric Cancer

The DisTinGuish study (NCT04363801) is a Phase 2 study of DKN-01 in combination with tislelizumab and standard of care (SOC) chemotherapy in patients with inoperable, locally advanced, G/GEJ adenocarcinoma. Part C of the DisTinGuish study will enroll approximately 160 first-line, HER2-negative patients who have had no prior therapy for unresectable locally advanced or metastatic G/GEJ adenocarcinoma. Patients will be randomized 1:1 to study DKN-01 in combination with tislelizumab and SOC chemotherapy, compared to tislelizumab and SOC chemotherapy. The primary objective of Part C is progression-free survival (PFS) in patients whose tumors express high levels of DKK1 (DKK1-high). Secondary objectives of Part C include PFS in all patients regardless of DKK1 expression, as well as overall survival (OS) and objective response rate (ORR) as measured by RECIST v1.1 in DKK1-high and all patients.

Part A and Part B of the DisTinGuish study are currently being conducted in the United States and the Republic of Korea. Part A enrolled 25 first-line HER2- G/GEJ cancer patients. As of December 10, 2021, the median PFS for all patients in Part A was 10.7 months, with 11.9 months PFS for DKK1-high patients, and the ORR for all patients who had completed a full cycle of therapy was 68%, with 90% ORR for DKK1-high patients. Part B of the study has enrolled 51 patients with second-line DKK1-high G/GEJ cancer. Additional follow-up data from Part A is expected to be presented in the third quarter 2022 and from Part B in the fourth quarter 2022.

Colorectal Cancer

The DeFianCe study is a Phase 2 study of DKN-01 in combination with bevacizumab and SOC chemotherapy in patients with advanced colorectal cancer who have received one prior systemic therapy. The study is designed with an initial 20 patient cohort and to then expand into a 130 patient randomized controlled trial against bevacizumab and SOC chemotherapy. The primary objective is PFS. Secondary objectives include ORR, duration of response (DOR), and OS. The study is expected to enroll its first patient in the third quarter 2022.

Endometrial Cancer

The investigator-initiated trial of DKN-01 in combination with pembrolizumab is an open-label, Bayesian design, Phase 2 trial and will initially enroll 15 patients each into DKK1-high and DKK1-low cohorts. If the efficacy criteria is met in either or both of the 15 patient cohort(s), then the cohort(s) will be expanded by an additional 15 patients. The primary objective of the study is ORR. Secondary objectives include clinical benefit rate (CBR), PFS, OS, and DOR. The study is expected to enroll its first patient in the fourth quarter 2022.

Leap has previously studied DKN-01 as a monotherapy and in combination with paclitaxel in patients with endometrial cancer. In the group of 23 patients treated with DKN-01 monotherapy for whom DKK1 expression data was available, patients with DKK1-high tumors achieved 1 complete response and 1 partial response, along with greater ORR (25% vs. 0%), CBR (63% vs. 7%), and median PFS (4.3 months vs. 1.8 months [HR 0.26; 95 CI: 0.09, 0.75]) compared to patients with DKK1-low tumors. In the group of 24 patients treated with DKN-01 plus paclitaxel, 72% of whom had received three or more prior systemic therapies, DKK1-high patients had improved median PFS (5.4 months vs. 1.8 months [HR 0.34; 95% CI: 0.12, 0.97]) compared to DKK1-low patients.

About DKN-01

DKN-01 is a humanized monoclonal antibody that binds to and blocks the activity of the Dickkopf-1 (DKK1) protein. DKK1 modulates the Wnt/Beta-catenin and PI3kinase/AKT signaling pathways and has an important role in promoting tumor proliferation, metastasis, angiogenesis, and in mediating an immune suppressive tumor microenvironment through enhancing the activity of myeloid-derived suppressor cells and downregulating NK cell ligands on tumor cells. The U.S. Food and Drug Administration has granted DKN-01 Orphan Drug Designation for the treatment of gastric and gastroesophageal junction cancer and Fast Track Designation in combination with tislelizumab for the treatment of patients with gastric and gastroesophageal junction adenocarcinoma whose tumors express high DKK1 protein, following disease progression on or after prior fluoropyrimidine- and platinum- containing chemotherapy and if appropriate, human epidermal receptor growth factor (HER2)/neu-targeted therapy.

About the Leap/BeiGene Collaboration

Leap is conducting the DisTinGuish study as part of an exclusive option and license agreement with BeiGene for the development of DKN-01 in Asia (excluding Japan), Australia, and New Zealand. Leap retains exclusive rights for the development, manufacturing, and commercialization of DKN-01 for the rest of the world.

About Leap Therapeutics

Leap Therapeutics (Nasdaq: LPTX) is focused on developing targeted and immuno-oncology therapeutics. Leap's most advanced clinical candidate, DKN-01, is a humanized monoclonal antibody targeting the Dickkopf-1 (DKK1) protein. DKN-01 is being developed in patients with esophagogastric, gynecologic, colorectal, and prostate cancers. Leap has entered into a strategic collaboration with BeiGene, Ltd. for the rights to develop DKN-01 in Asia (excluding Japan), Australia, and New Zealand. For more information about Leap Therapeutics, visit http://www.leaptx.com or view our public filings with the SEC that are available via EDGAR at http://www.sec.gov or via https://investors.leaptx.com/.

FORWARD-LOOKING STATEMENTS

This press release contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, Section 21E of the Securities Exchange Act of 1934, as amended, and the Private Securities Litigation Reform Act of 1995, which involve risks and uncertainties. These forward-looking statements include statements regarding Leap's business strategies, collaborations and partnerships, and expectations with respect to the development and advancement of DKN-01 in clinical trials, including the outcomes, status and timing of current or future studies. Although Leap believes that the expectations reflected in such forward-looking statements are reasonable as of the date made, forward-looking statements are subject to known and unknown risks, uncertainties and other factors that could cause actual results to differ materially from our expectations. Such risks and uncertainties include, but are not limited to: the uncertain clinical development process, including the risk that clinical trials may not have an effective design or generate positive results; that the initiation, conduct, and completion of clinical trials, laboratory operations, manufacturing campaigns, and other studies may be delayed, adversely affected, or impacted by COVID-19 related issues; unstable global market and economic conditions; the accuracy of our estimates regarding expenses, future revenues, capital requirements and needs for financing; the benefits to be derived from our agreement with BeiGene, Ltd. ("BeiGene") or any other collaborations, license agreements, or other acquisition efforts; the rate and degree of market acceptance of DKN-01; the success of other competing therapies that may become available; the manufacturing capacity for DKN-01; our ability to maintain and protect our intellectual property rights; and other risks and uncertainties. Detailed information regarding factors that may cause actual results to differ materially from expectations is included in Leap Therapeutics' periodic filings with the SEC, including Leap's Annual Report on Form 10-K for the fiscal year ended December 31, 2021, as filed with the SEC on March 11, 2022 and as may be updated by Leap's Quarterly Reports on Form 10-Q and the other reports Leap files from time to time with the SEC. Any forward-looking statement contained in this release speaks only as of its date. Leap undertakes no obligation to update any forward-looking statement contained in this release to reflect events or circumstances occurring after its date or to reflect the occurrence of unanticipated events.

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