Initial Results from Ongoing Dose-Escalation Study of XmAb819 & Oncology Pipeline Update

October 24, 2025

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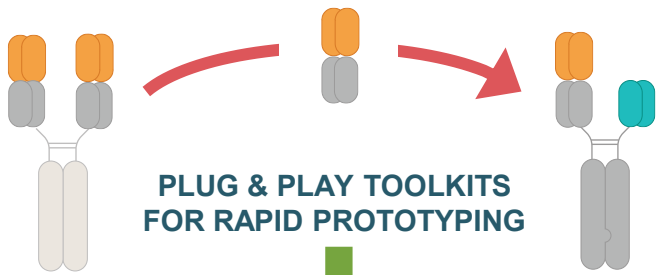
Proven Power of XmAb® Engineering: Proteins By Design®

Small changes, big functional impacts

- XmAb Fc Domains augment native immune functions in molecules and/or control their structure, while preserving desired attributes
- XmAb engineered antibodies are designed to solve complex biologic problems
- Strong patent portfolio



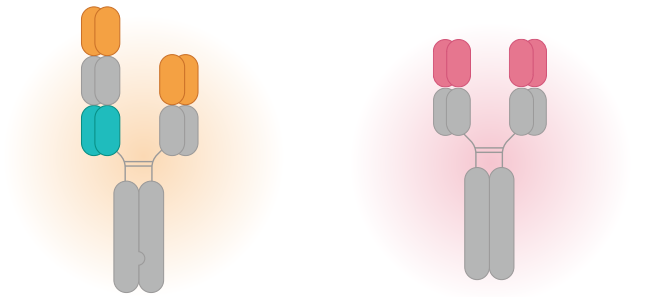
Advancing an optimized portfolio of XmAb drug candidates

Oncology: Advancing a portfolio novel TCEs

- **XmAb819** (ENPP3xCD3) in advanced ccRCC: enrolling first Phase 1 dose expansion cohort
- **XmAb541** (CLDN6xCD3) in ovarian cancer and GCTs: ongoing Phase 1 dose escalation

Autoimmune: anti-TL1A and CD3 B-cell depletion

- **XmAb942** (TL1A): XENITH-UC 2b study ongoing
- **XmAb412** (TL1A x IL23p19): Ph1 to initiate in 2026
- **Plamotamab** (CD20xCD3): Ph1 RA study ongoing
- **XmAb657** (CD19xCD3): Ph 1 to initiate in 4Q'25



XmAb Bispecific TCEs

Xtend™ Antibodies with Potential Best-in-class Half-life Extension

Partnerships leverage modular XmAb technology

- More than 15 technology license partnerships greatly broadens scope with little-to-no effort
- Multiple commercialized XmAb antibodies

ULTOMIRIS® **MONJUVI®/MINJUVI®**

COLLABORATION PORTFOLIO INCLUDES

Johnson&Johnson Innovative Medicine · AMGEN · ALEXION AstraZeneca Rare Disease · Incyte · Genentech A Member of the Roche Group · GILEAD · VIR · astellas

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TCE T-cell engager **ccRCC** clear cell renal cell carcinoma
GCT germ cell tumor **RA** rheumatoid arthritis **UC** ulcerative colitis

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Next-Gen XmAb® Drug Design in Oncology & Autoimmune Diseases

Pipeline focus on T-cell engagers and bispecific mechanisms

Program	Targets	XmAb® Platforms	Indications	Discovery	Preclinical	Phase 1	Phase 2	Phase 3
Solid Tumor Oncology: T-cell Engagers (CD3 & CD28)								
XmAb819	ENPP3 x CD3	2+1 Bispecific	ccRCC					
XmAb541	CLDN6 x CD3	2+1 Bispecific, Xtend™	Ovarian cancer, GCT, oncology					
XmAb808	B7-H3 x CD28	2+1 Bispecific, Xtend	Prostate cancer, oncology					
XmAb Program	Undisclosed TCE	Bispecific, Xtend	Solid tumor oncology					
Immunology Programs (TL1A & CD3 B-Cell Depletion)								
XmAb942	TL1A	Xtend, FcKO	IBD (Ulcerative colitis)				Phase 2b XENITH-UC	
XmAb412	TL1A x IL23p19	Bispecific, Xtend	IBD				2026	
Plamotamab	CD20 x CD3	Bispecific	Rheumatoid Arthritis				Phase 1b	
XmAb657	CD19 x CD3	2+1 Bispecific, Xtend	Autoimmune Diseases				2H'25	

Key: Solid tumors | Immunology | Planned Study Initiation

ccRCC clear cell renal cell carcinoma **GCT** germ cell tumors **FcKO** Fc knock out **IBD** Inflammatory bowel disease

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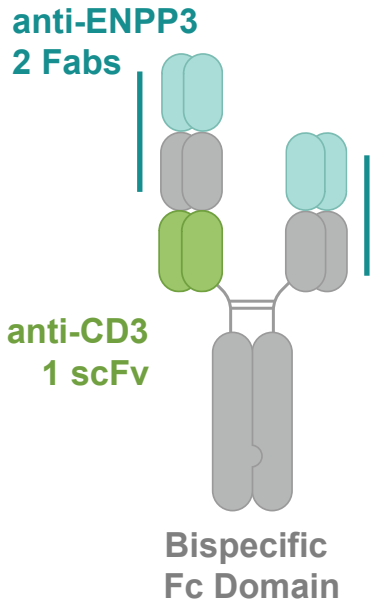
XmAb819: ENPP3 x CD3 T-cell Engager in Development for ccRCC

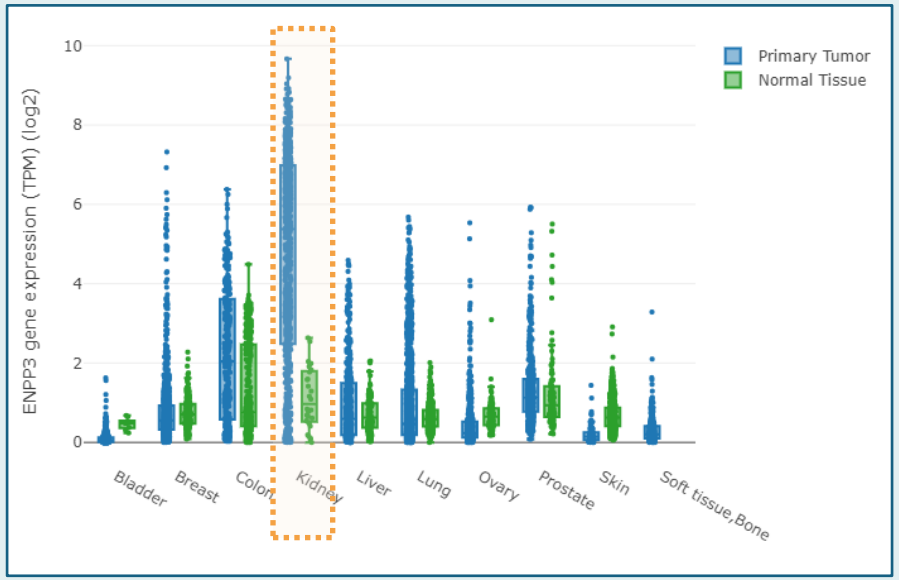
XmAb819 engages the immune system and activates T cells for highly potent and targeted lysis of tumor cells expressing ENPP3



ENPP3

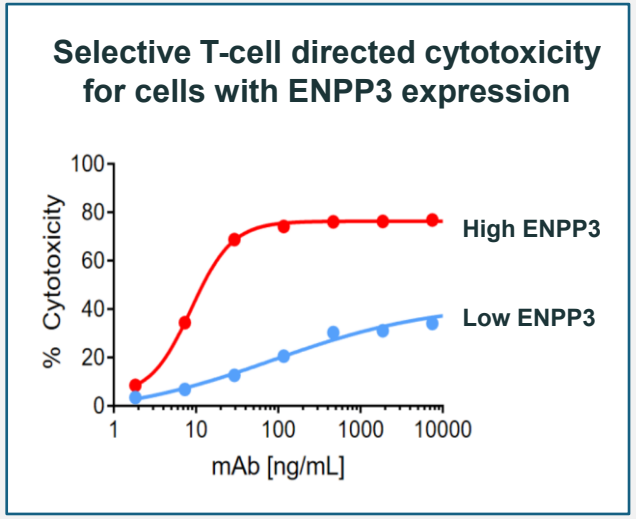
Ectonucleotide pyrophosphatase / phosphodiesterase family member 3

A differentially expressed target, with high level expression in renal cell carcinoma and low-level expression on normal tissues[1]



XmAb® 2+1

Enables antibodies to bind more avidly and selectively kill tumor cells with higher antigen density, potentially sparing normal cells



1 Doñate, Fernando, et al. Clinical Cancer Research 22.8 (2016)

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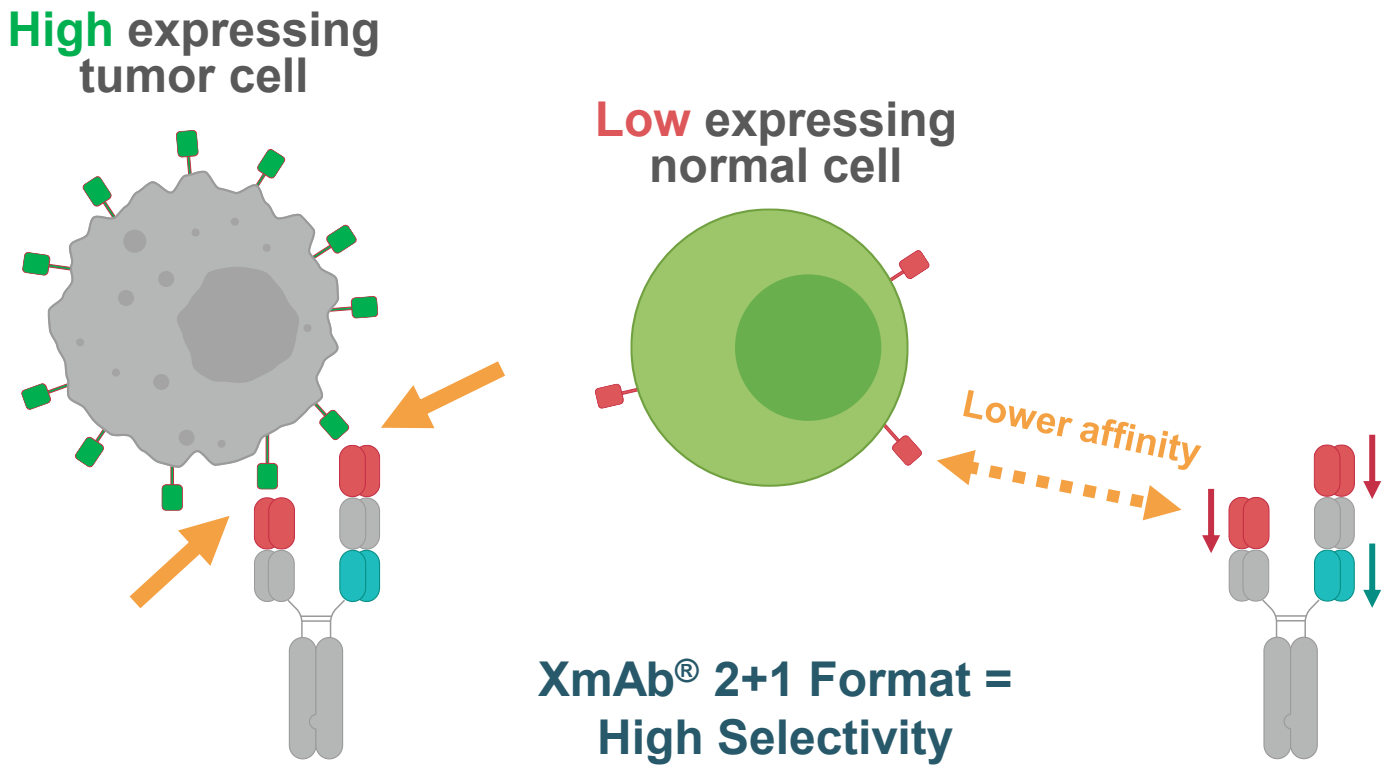
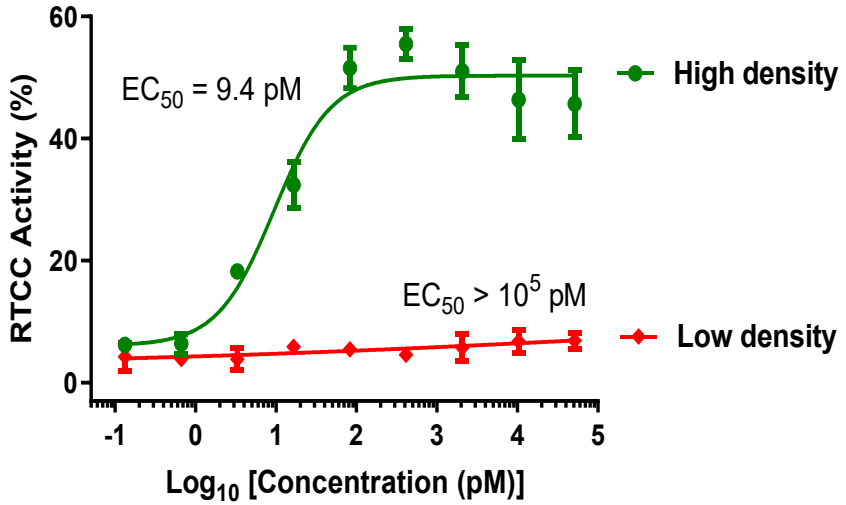
2+1 Bispecifics: XmAb® T Cell Engagers Use Multiple Formats and Affinity Designs to Customize for Each Tumor Target





Examples of XmAb 2+1 TCEs: xaluritamig (STEAP1), ASP2138 (CLDN18.2), XmAb819 (ENPP3), XmAb541 (CLDN6)

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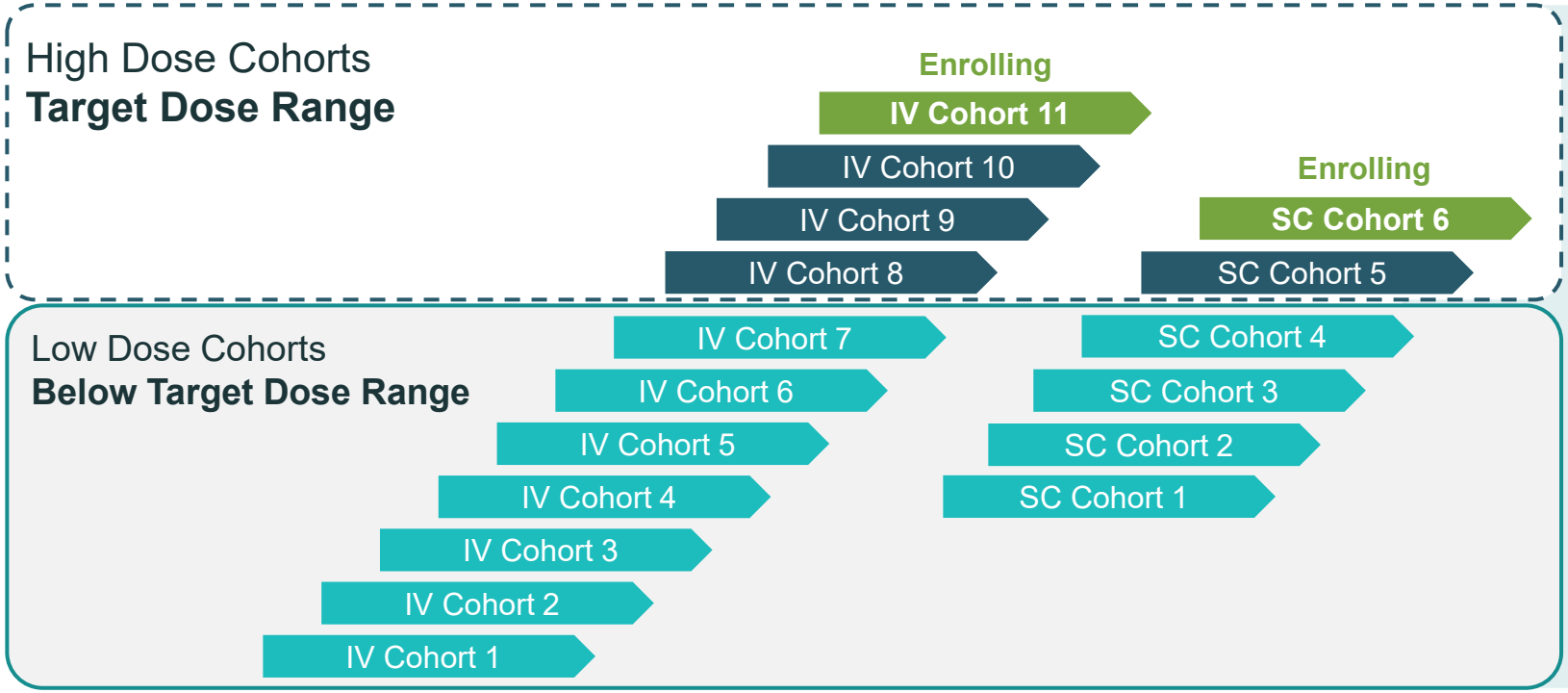
Ongoing Phase 1 Dose-Escalation of XmAb819 in ccRCC

Initial Results

Data Cut-off: September 19, 2025

XmAb819 Phase 1 Dose Escalation: Parallel IV and SC Design

Study Schema and Dosing Schedule



Key Eligibility Criteria

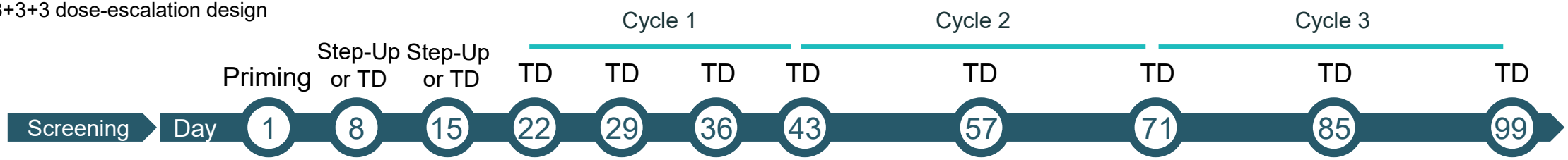
- ≥ 18 years
- R/R ccRCC – prior CPI & VEGF TKI
- Measurable disease by RECIST v1.1
- No prior anti-ENPP3 therapy

Objectives

- Safety and tolerability
- Identify recommended dose
- Pharmacokinetics
- Anti-tumor activity

NCT05433142

3+3+3 dose-escalation design



TD Target Dose **CPI** checkpoint inhibitor

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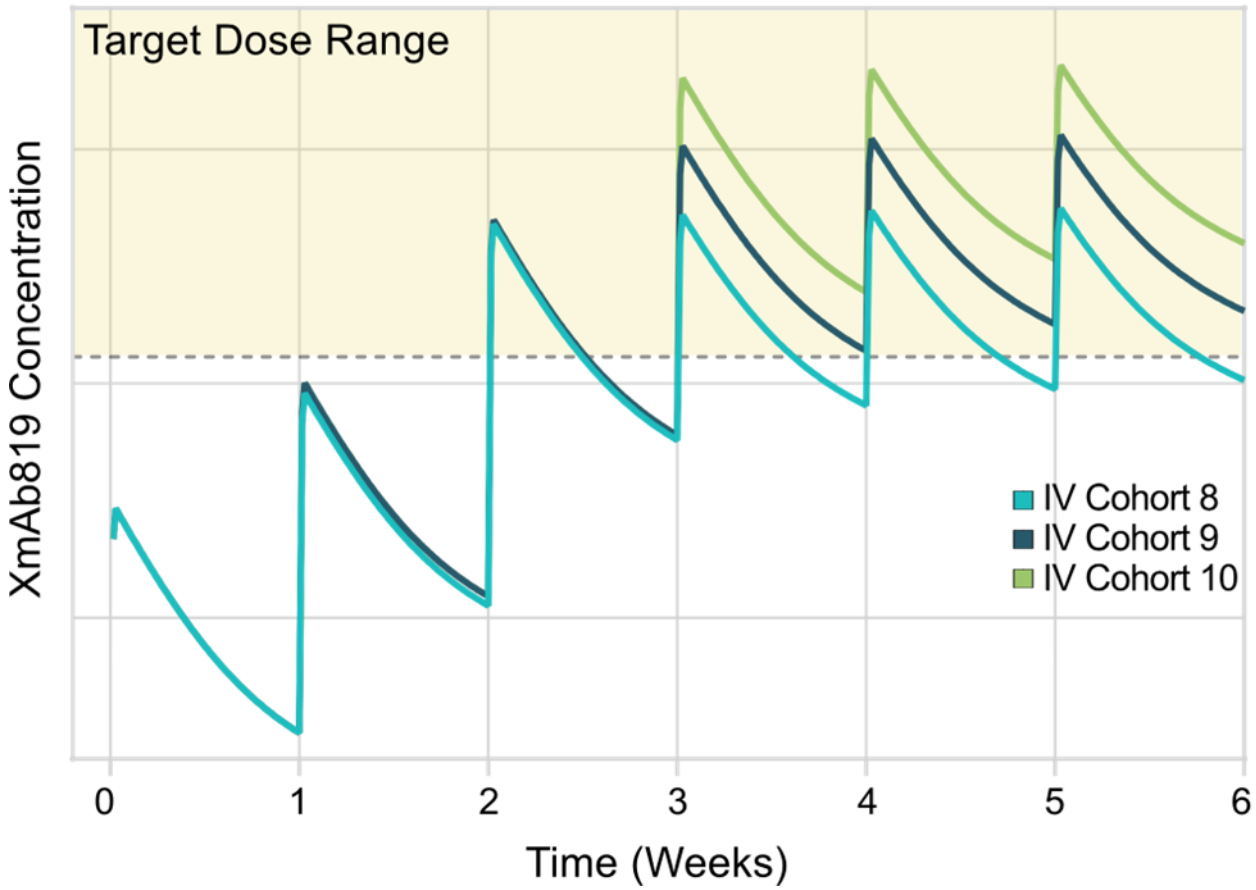
Pharmacokinetic Profile of XmAb819 Supports QW - Q2W Dosing



Parameter	Value
Half-life	8.7 Days
Subcutaneous Administration	
T_{max}	5.5 Days
Absolute Bioavailability	55-70%

Steady state drug concentrations attained in Cohorts 9 and 10 fall within the PK target dose range expected to achieve anti-tumor activity

PK pharmacokinetics

Heavily Pre-treated Patient Population in Ongoing Dose Escalation

Baseline Characteristics	
N	69
Median age, Years (Min, Max)	60 (34, 77)
Male, n (%)	55 (80)
Race, n (%)	
White	61 (88)
Other	8 (12)
Time since initial diagnosis, Months (Min, Max)	53.6 (8, 259)
IDMC risk score at initial diagnosis, n (%)	
Favorable	22 (32)
Intermediate	19 (28)
Poor	9 (13)
Not Available	19 (28)
Sarcomatoid features, n (%)	7 (10)

Prior Therapy	
N	69
# Prior regimens, Median (Min, Max)	4 (1, 8)
1, n (%)	5 (7)
2	16 (23)
3	13 (19)
4	9 (13)
≥5	26 (38)
Prior treatments, n (%)	
Checkpoint inhibitor	69 (100)
VEGF TKI	69 (100)
2 or more TKI	42 (61)
HIF2α inhibitor	25 (36)
Prior Nephrectomy, n (%)	47 (68)

IDMC International Metastatic RCC Database Consortium **VEGF** vascular endothelial growth factor **TKI** tyrosine kinase inhibitor **HIF2a** hypoxia-inducible factor 2-alpha

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Low Rate of Discontinuations Due to Adverse Events

Patient Disposition	
N	69
Treatment Status, n (%)	
Ongoing	17 (25)
Discontinued	52 (75)
Reason for Treatment Discontinuation, n (%)	
Adverse event*	3 (4)
Physician decision	3 (4)
Subject declines further treatment	2 (3)
Progressive disease	38 (55)
Clinical progression	6 (9)

* Elevated liver enzymes (n=1), non-fatal myocardial infarction in the presence of hypotension and CRS (n=1), AST/ALT increased (n=1)

CRS cytokine release syndrome **AST** aspartate aminotransferase **ALT** alanine aminotransferase

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Safety Summary – Well-tolerated Treatment With >90% of Patients Reaching Target Dose; Low Rate of Discontinuation

Treatment Emergent Adverse Events (TEAE), n (%)	
N	68 (99)
Grade ≥3	48 (70)
Related Grade ≥3	31 (45)
Serious TEAE	35 (51)
Related Serious TEAE	28 (41)
Lead to Dose Reduction	4 (6)
Did Not Reach Target Dose	6 (9)
Lead to Treatment Discontinuation	3 (4)
Lead to Death	0

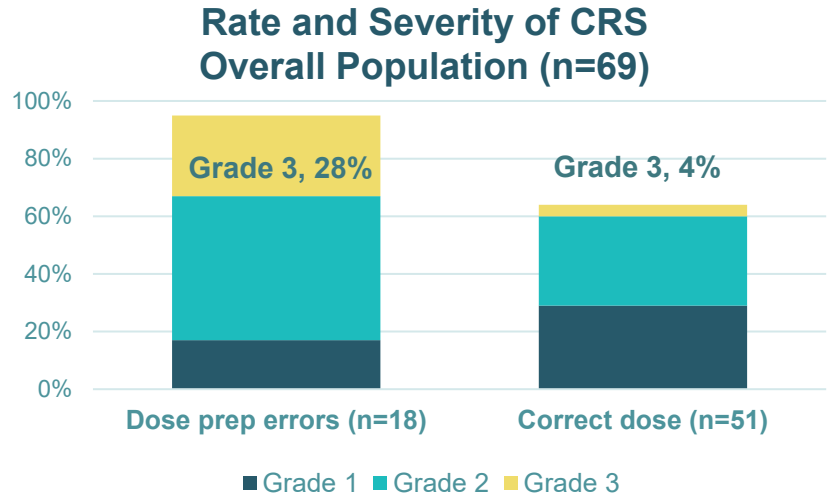
CRS Profile Primarily Low Grade and Occurs in Initial Priming Doses

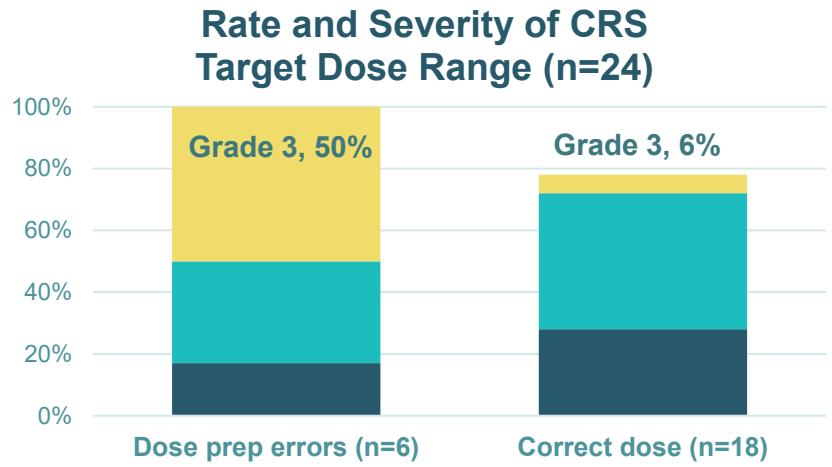
Correct dose preparation resulted in 4% Grade 3 CRS (2/51), whereas dose preparation errors resulted in 28% Grade 3 CRS (5/18)

In the target dose range, correct dose preparation resulted in 6% Grade 3 CRS (1/18), whereas dose preparation errors resulted in 50% Grade 3 CRS (3/6)

- Port and syringe errors diluting XmAb819 drug product during the priming dose preparation led to higher drug exposure (3-8x) in some patients after the priming dose
- Errors correlated to Grade 3 CRS and step-up dosing delays
- Mitigation through site retraining completed

Eliminating root cause of multiple dilution steps with low concentration drug product rollout in 1H 2026

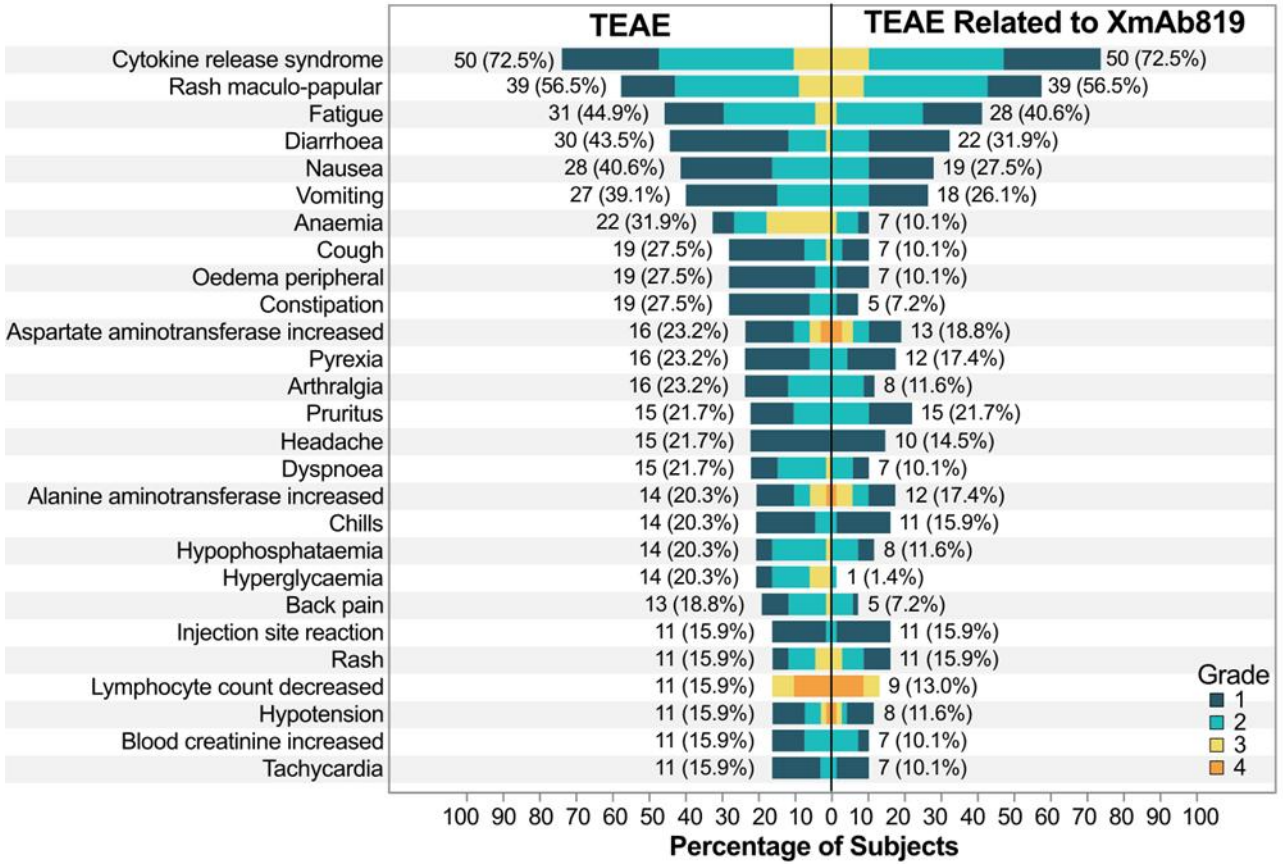




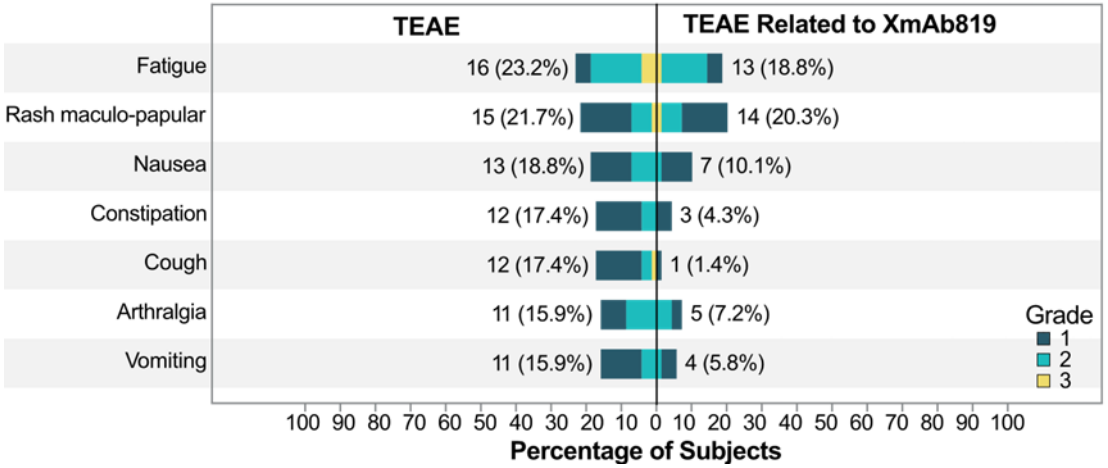
CRS cytokine release syndrome

AEs Primarily During the Priming Period and Well Managed With Low Overall Rate at Target Doses

Overall TEAE and Related TEAE by Maximum Severity Grade (N=69)



>Day 29 to End of Study TEAE and Related TEAE by Maximum Severity Grade (N=69)



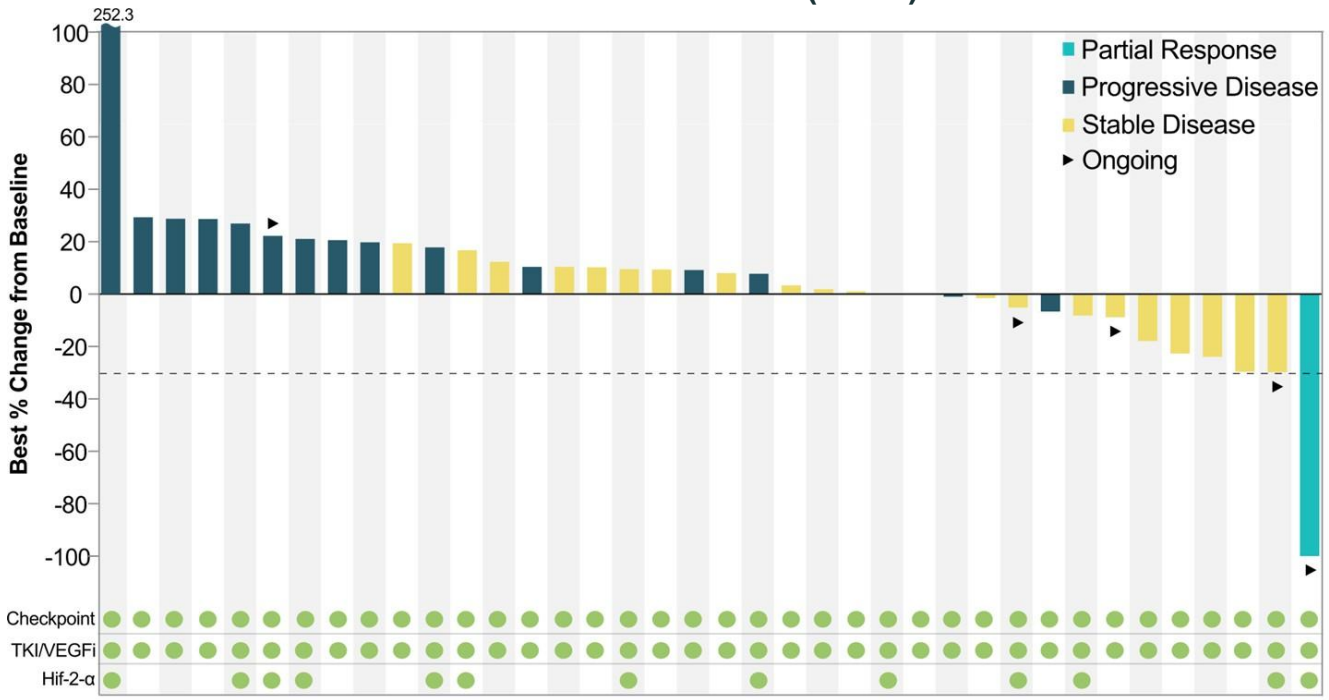
Most common AEs are CRS and rash

- Majority of CRS events are Grade 1/2 and occur during priming
- Rash events are mostly Grade 1/2; responsive to antihistamines and steroids (topical/oral)

Clear Evidence of XmAb819 Dose Response in Ongoing Dose Escalation of Heavily Pre-Treated Patients

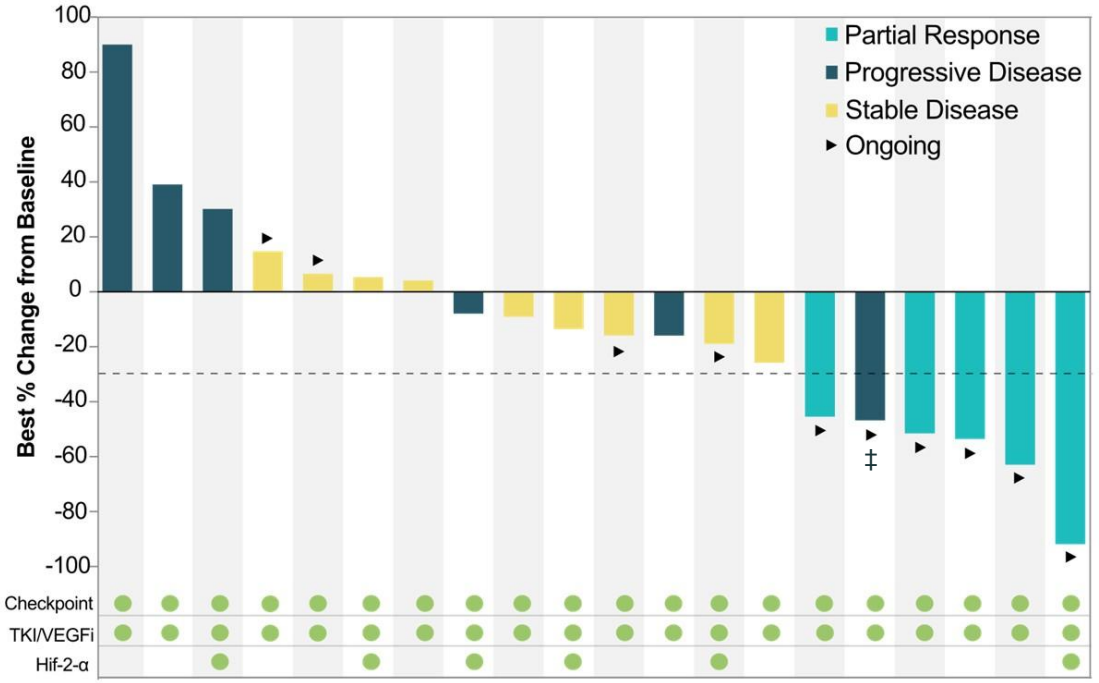
Best Percent Change from Baseline in Tumor Lesion (RECIST 1.1)

Low Dose Cohorts (N=38)*



* Excludes 4 patients without post-baseline scans and 3 patients with non-evaluable post-baseline measurements

Target Dose Cohorts (N=20)†



† Excludes 3 patients without post-baseline scans and 1 patient with non-evaluable post-baseline measurements

‡ PD at first scan (D48) prior to receiving target dose on D50. Continued treatment post-progression resulted in 47% tumor reduction. Continues on study at week 30.

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Best Overall Response Supports Monotherapy Development

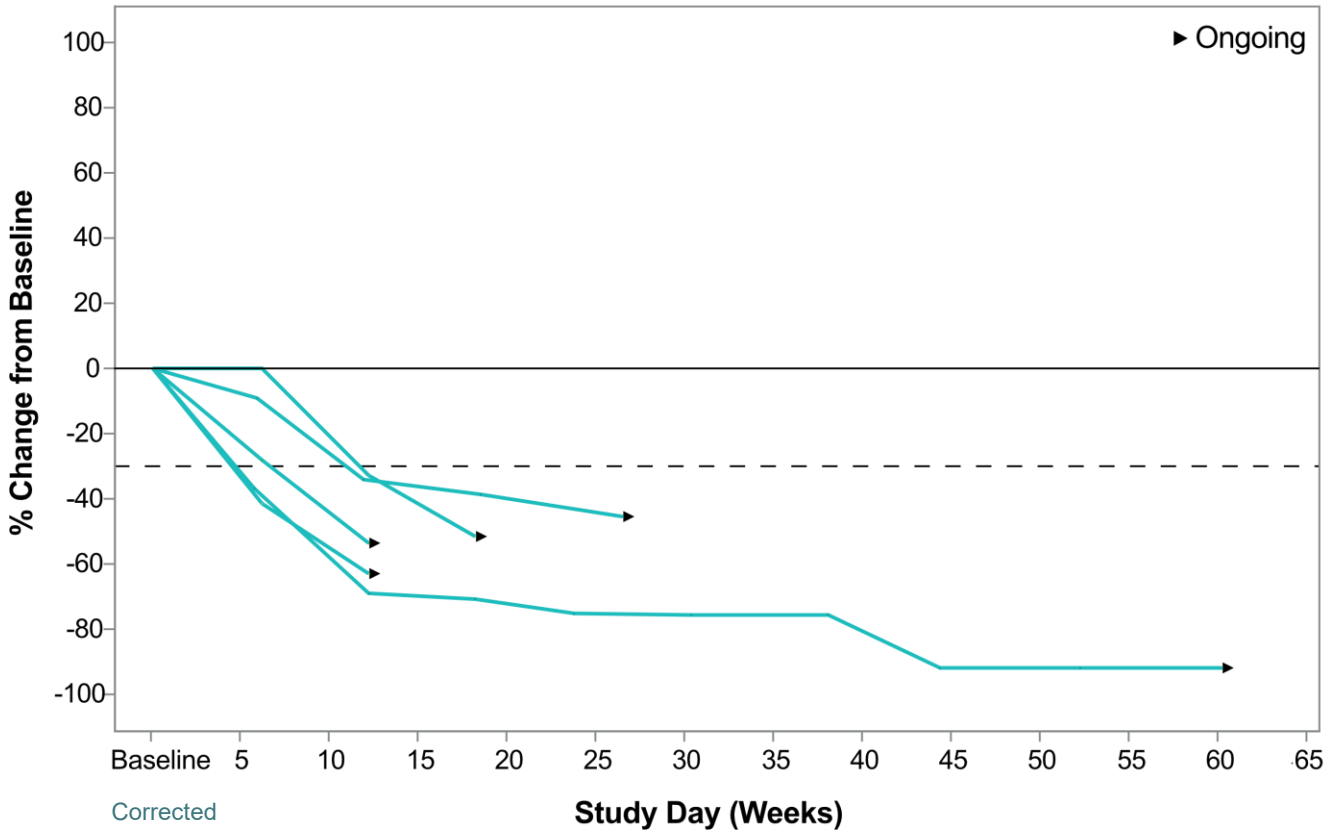
All Responders Treatment Ongoing

Best Overall Response in the Efficacy Evaluable Target Dose Range	
N	20*
Objective Response Rate (ORR), % (95% CI)	25% (9, 49)
Complete Response (CR)	0
Unconfirmed Partial Response (uPR) / Confirmed Partial Response (cPR)†, n (%)	5 (25)
Stable Disease (SD), n (%)	9 (45)
Disease Control Rate (DCR), % (95% CI)	70% (46, 88)

* Excludes 3 patients without post-baseline scans and 1 patient with non-evaluable post-baseline measurements.

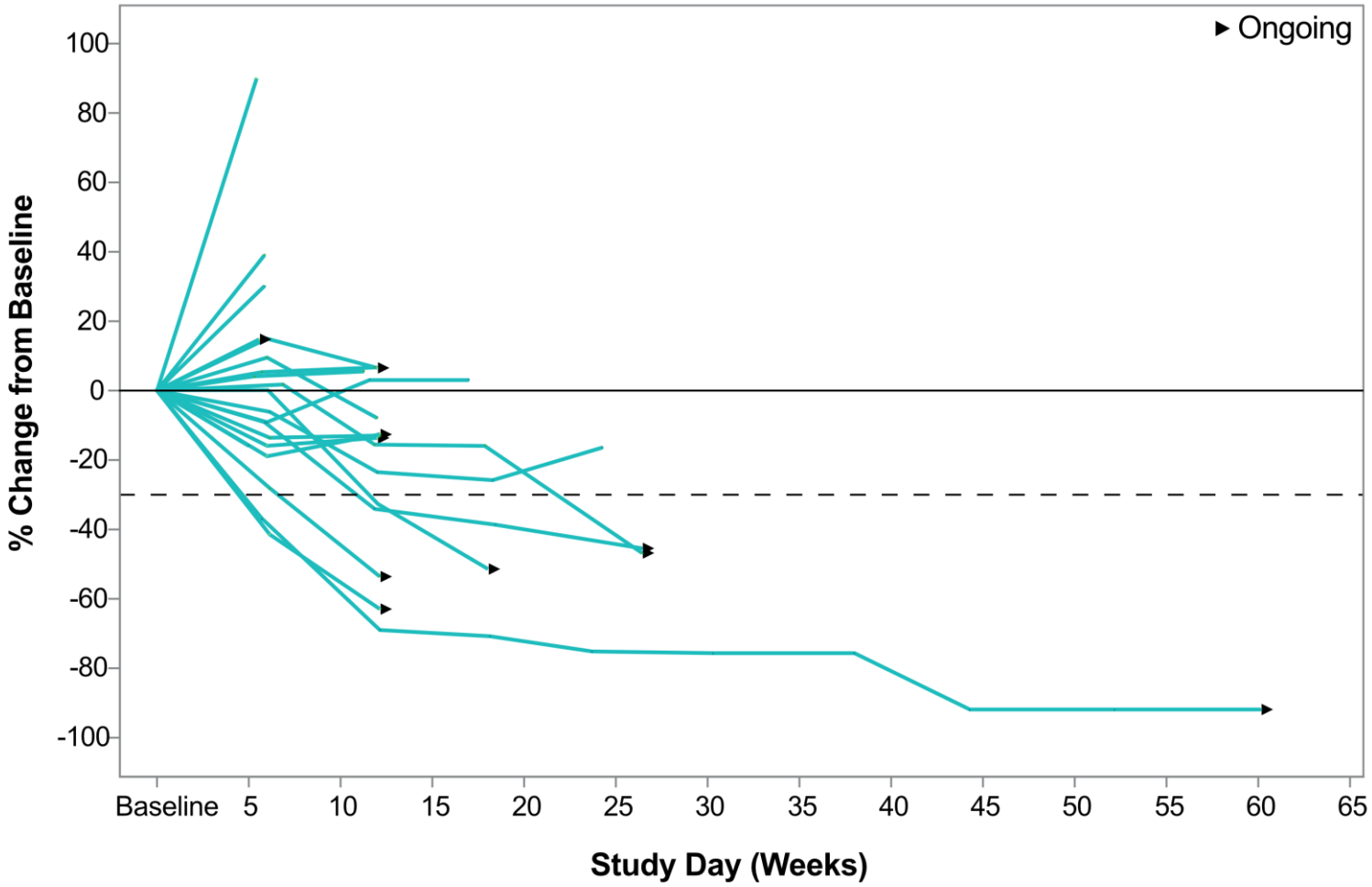
† 4 cPR. 1 uPR deemed not evaluable after PR (54% reduction in target lesions at week 12) due to subsequent radiation to symptomatic non-target lesion with target lesion in field. The patient continues on treatment with stable scan at week 36.

Percent Change from Baseline in Tumor Lesion Responders in Target Dose Range



Majority of Patients Experience Reduction in Tumor Lesions

Percent Change from Baseline, Target Dose Range (N=20)



Corrected

Excludes 3 patients without post-baseline scans and 1 patient with non-evaluable post-baseline measurements

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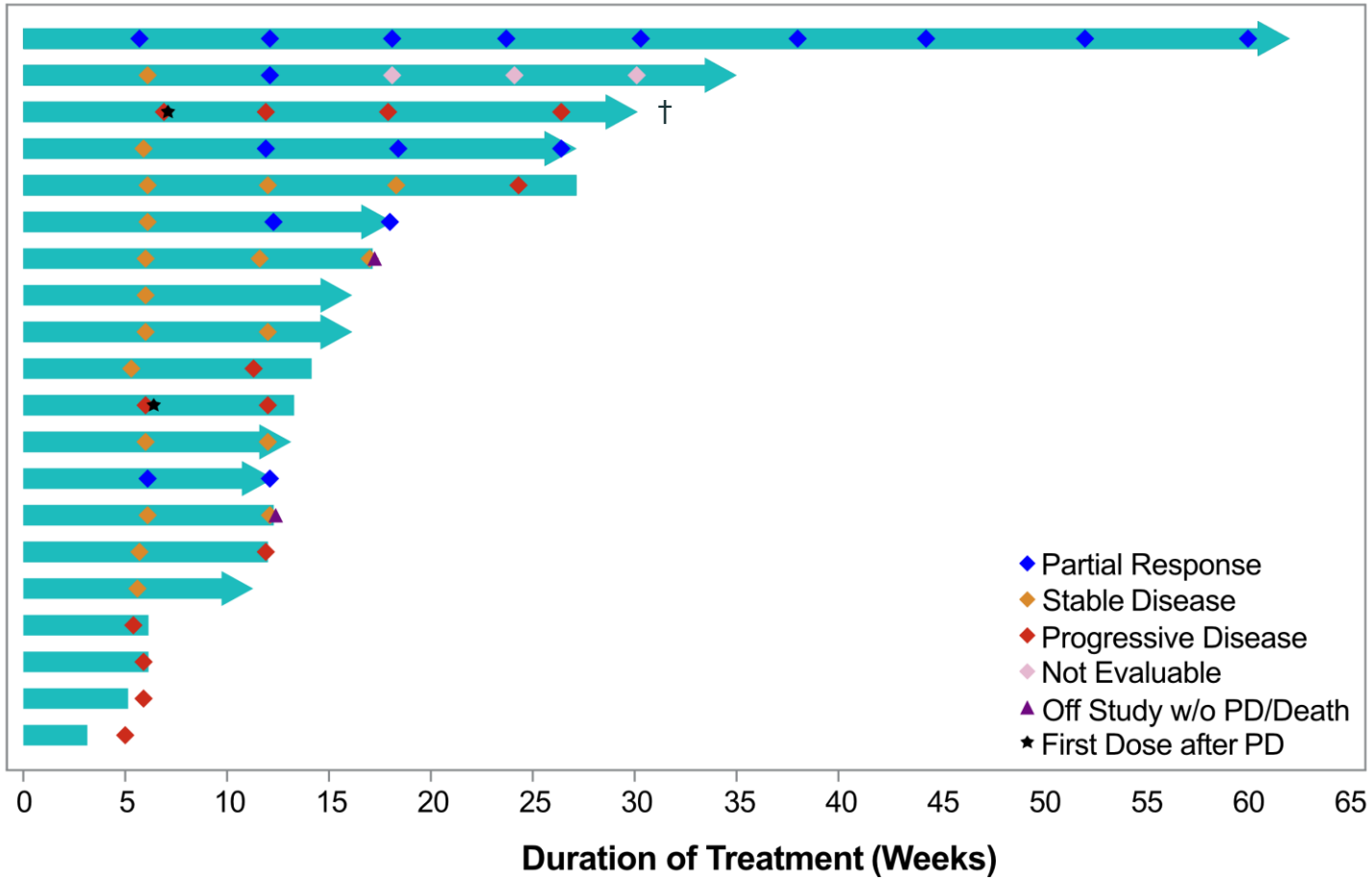
XmAb819 Treatment Has Resulted in Sustained Disease Control

Response by Subject, Efficacy Evaluable (RECIST 1.1)
Target Dose Range (N=20)



Corrected

† PD at first scan (D48) prior to receiving target dose on D50. Continued treatment post-progression resulted in a 47% tumor reduction.

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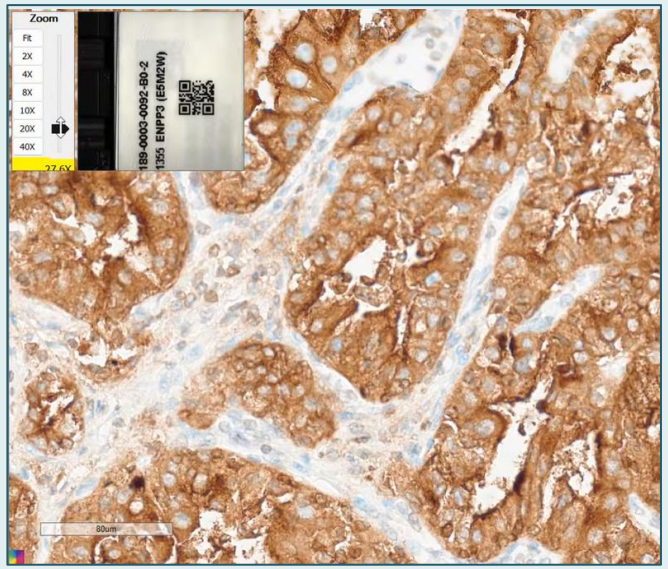
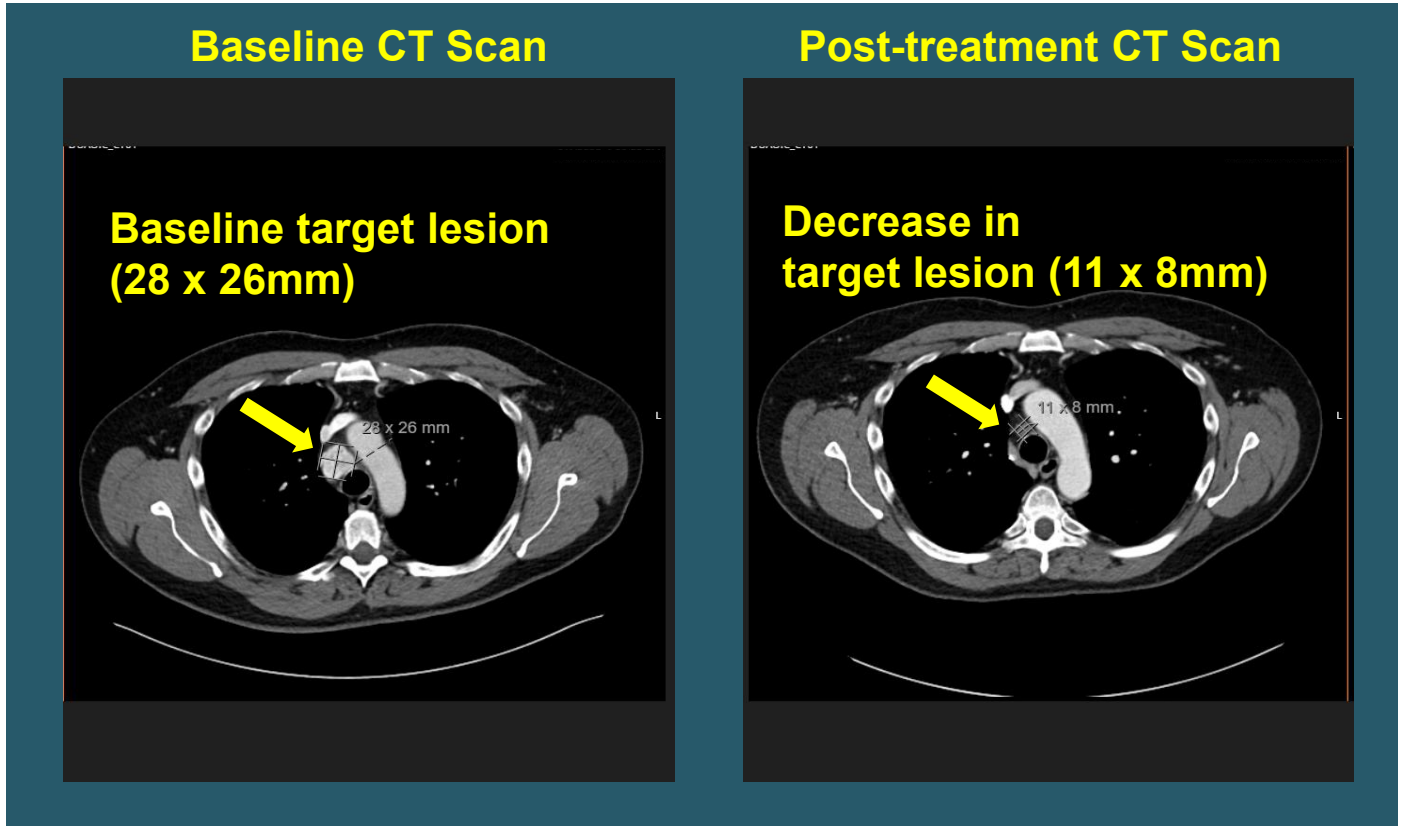
Case Example: ~63% Target Lesion Reduction Despite Membrane TPS<25% Indicates Potential Bystander Effect

- 56-year-old male diagnosed ~10 years ago; metastatic disease less than 5 years ago
- 2 prior lines of therapy: cabozantinib/nivolumab (1 month), lenvatinib/everolimus (3 years)



- Membrane ENPP3+ in <25% tumor
- Diffuse cytoplasmic staining



TPS Tumor Proportion Score

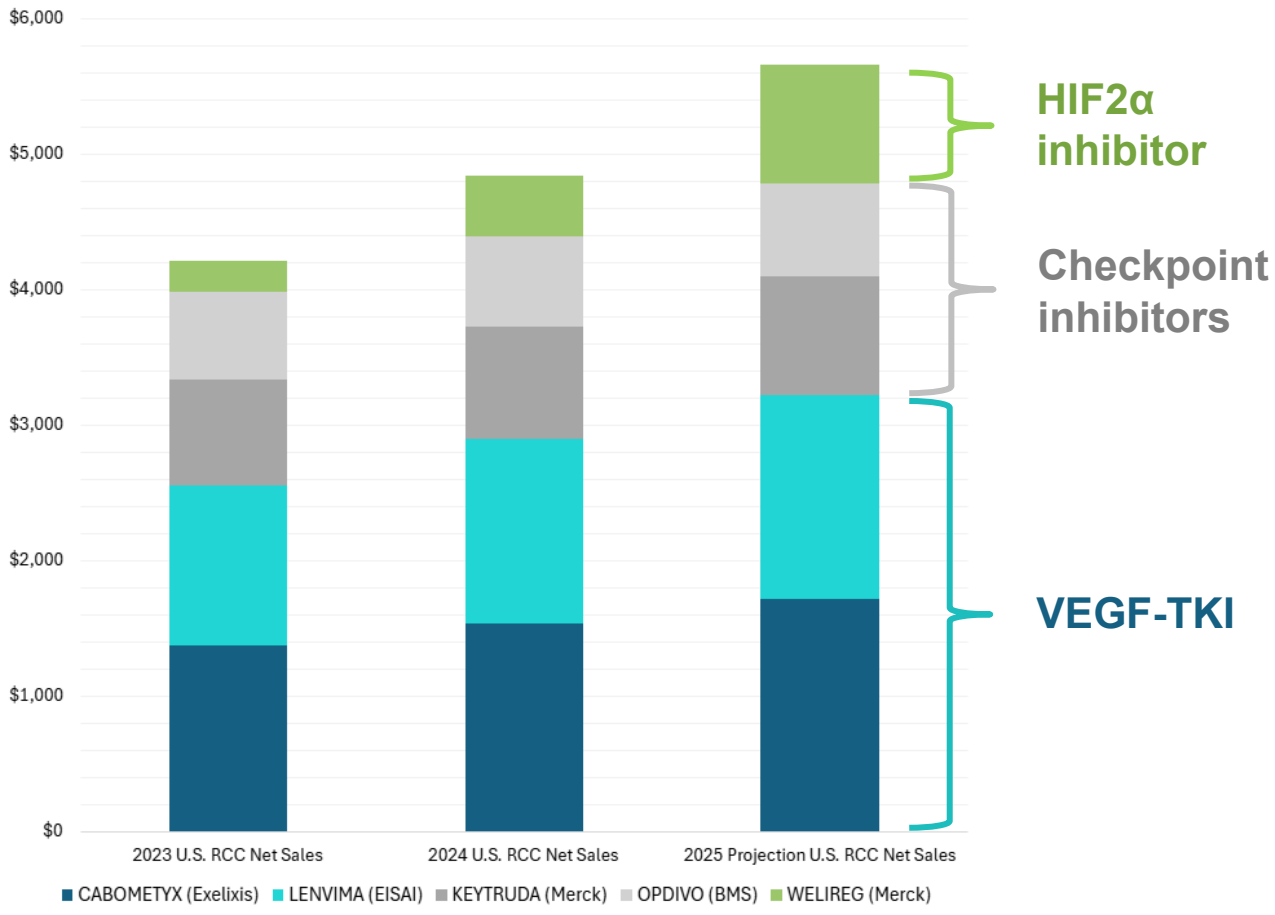
Competitive Positioning & Commercial Opportunity

XmAb819 On-track for ccRCC Pivotal Study Start During 2027

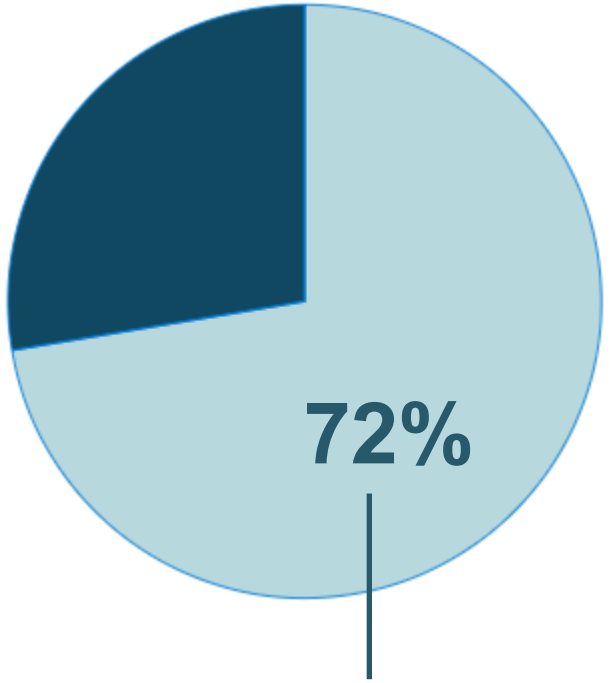
- Achieved 25% ORR in unselected, heavily pretreated ccRCC patients, meeting internal criteria for progression to dose-expansion phase ✓
- Well-tolerated safety profile observed with mainly Grade 1/2 CRS, transient rash and liver enzyme elevations, no ICANS; patients beyond Day 29 show low incidence of mild AEs ✓
- Enrollment at IV Expansion Dose 1 has initiated; dose escalation continues to identify IV Expansion Dose 2 — 2026
- Determination of optimal IV or SC administration route and RP3D decision — 2026
- Expansion into additional tumor types and combination studies with existing SoC in ccRCC, following establishment of the monotherapy RP3D — 2026 2027

Size of Global RCC Market Expected to Reach ~$12B in 2030 With Limited 2L+ Treatment Options Beyond VEGF-TKI[1]

RCC U.S. Net Sales ($M)[1,2]



U.S. Total Addressable Market (TAM) in RCC in 2025



Aggregate U.S. Net Sales of Cabometyx® + Lenvima® + Welireg® in RCC[1,2]

1 GlobalData **2** Company earnings reports

Registered trademarks: Cabometyx (Exelixis, Inc.), Lenvima (Eisai R&D Management Co., Ltd.), Keytruda & Welireg (Merck Sharp & Dohme LLC), Opdivo (Bristol-Myers Squibb Company)

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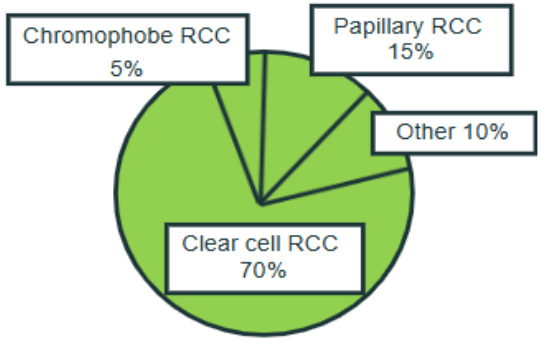
Opportunity for a Novel First-in-class T-cell Engager to Improve SoC for Patients With Advanced ccRCC

US ccRCC incidence
~ 60k[1] new cases per year

Global Incidence[2]: ~435k/year



1st Line

~ 20k addressable U.S. patients

IO + IO

Nivo+Ipi

IO + VEGF-TKI

Nivo+Cabo
Pembro+Lenva
Pembro+Axitinib
Avelumab+Axitinib

50%[3]

2nd Line

~ 10k addressable U.S. patients

VEGF-TKI

Cabozantinib
Tivozanib
Lenvatinib ± everolimus

50%[3]

3rd Line

~ 5k addressable U.S. patients

HIF2α inhibitor post IO + VEGF-TKI (LITESPARK-005)

Belzutifan

1 SEER **2** GLOBOCAN 2022 **3** Ozay ZI et al. Treatment and Attrition Trends for Metastatic Clear Cell Renal Cell Carcinoma in the US. JAMA Netw Open.
SoC standard of care **Nivo** nivolumab **Ipi** ipilimumab **Prembro** pembrolizumab **Lenva** lenvatinib

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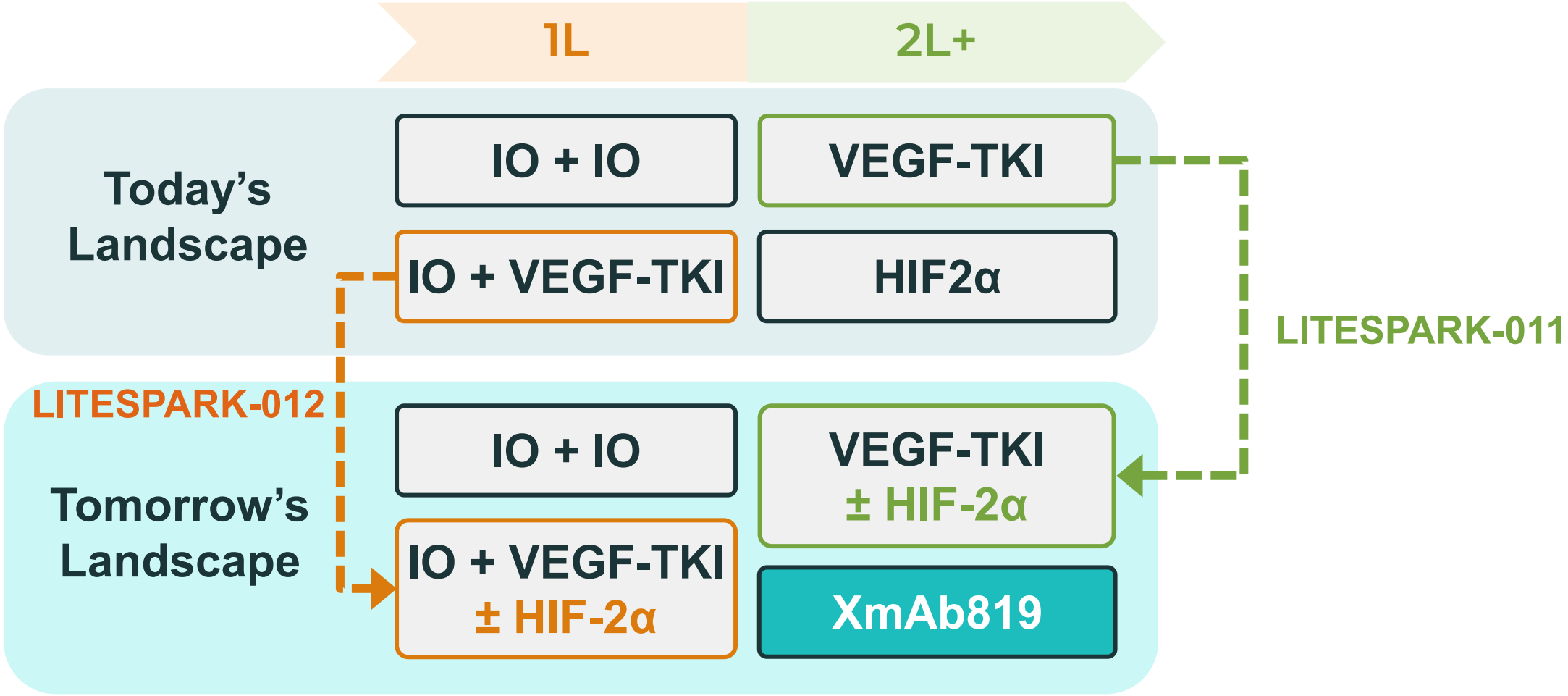
Evolving ccRCC Landscape Has Opportunity to Redefine SoC with XmAb819 in 2L+ Post IO and VEGF-TKI Treatment



1 Choueiri, et al. Nature medicine 27.5 (2021): 802-805. **2** ESMO 2023 Presentation from Dr. Albiges. **3** Rini, et al. The Lancet Oncology 21.1 (2020): 95-104.

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XmAb819 Preliminary Efficacy Demonstrates Potential to Advance SoC for Patients That Have Progressed After CPI and VEGF-TKI Treatment

Drug	XmAb819	Belzutifan	Belzutifan	Tivozanib
Study	**Preliminary Dose Escalation**	**Phase 1 Dose Expansion (ccRCC)[1]**	**IA1 & IA2 for LITESPARK-005[2]**	**TIVO-3 Study[3]**
Efficacy Evaluable, N	20	55	374	175
Overall Response Rate (ORR), % (95% CI)	**25% (9-49)**	**25% (15-39)**	**23% (19-27)**	**18% (12-24)**
Complete Response (CR)	0%	0%	4%	0%
Partial Response (PR)	25%	25%	19%	18%
Stable Disease (SD)	45%	54%	38%	55%
Disease Control Rate (DCR)	**70%**	**80%**	**61%**	**73%**
Baseline Characteristics, N	69	55	374	175
Prior Regimens, Median (Range)	**4 (1-8)**	**3 (1-9)**	**2 (1-4)**	**2 (2-3)**
1, %	7%	15%	12%	0%
2	23%	24%	42%	62%
≥3 prior regimens	**70%**	**62%**	**45%**	**38%**
3	19%	≥3 prior 62%	45%	38%
4	13%	NA	1%	0%
≥5	38%	NA	0%	0%
Prior treatments, %				
Checkpoint inhibitor	100%	80%	100%	27%
VEGF TKI	100%	91%	100%	100%
2 or more TKI	61%	NA	50%	45%
HIF2α inhibitor	36%	0%	0%	0%

1 Choueiri, et al. Nature medicine 27.5 (2021): 802-805. **2** ESMO 2023 Presentation from Dr. Albiges. **3** Rini, et al. The Lancet Oncology 21.1 (2020): 95-104.

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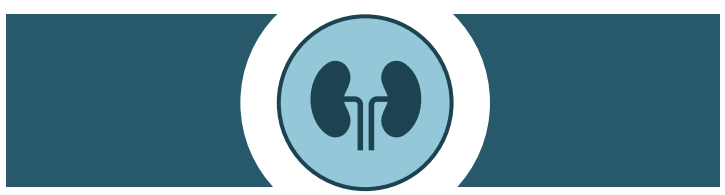
Strategic Expansion Opportunities for XmAb819 Beyond ccRCC

ENPP3+ patients in 2L/3L+ setting[1] of pRCC, CRC & NSCLC **~60K**



Papillary RCC

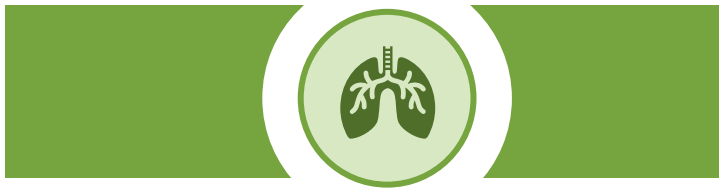
Standard of care
Cabozantinib

Treatable patients
~6K

MSS Colorectal Cancer

Standard of care
Regorafenib or Fruquitinib or FTD/TPI + Bevacizumab

Treatable patients
~13K



NSCLC Adenocarcinoma

Standard of care
Docetaxel

Treatable patients
~40K

1 Estimates for U.S. 2025 ENPP3 population based upon H-Score of ≥1

MSS microsatellite stable **NSCLC** non-small cell lung cancer

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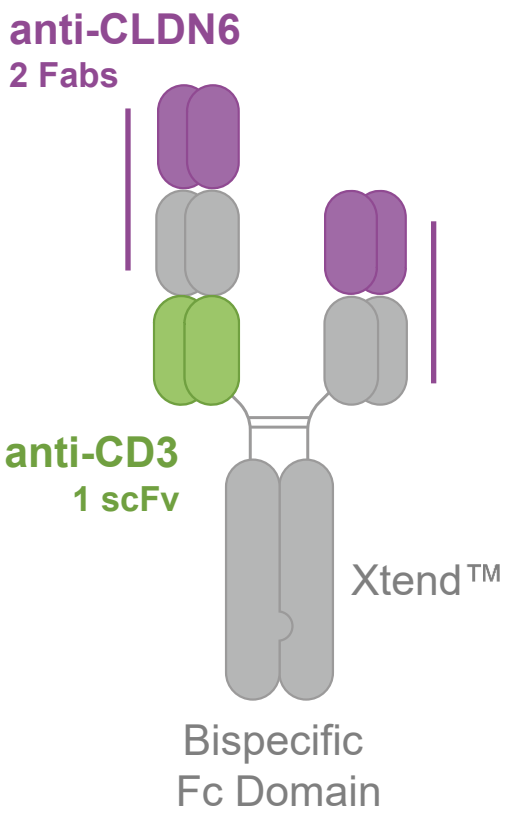
Early Look at XmAb541 in Advanced Ovarian Cancer, Endometrial Cancer and Germ Cell Tumors

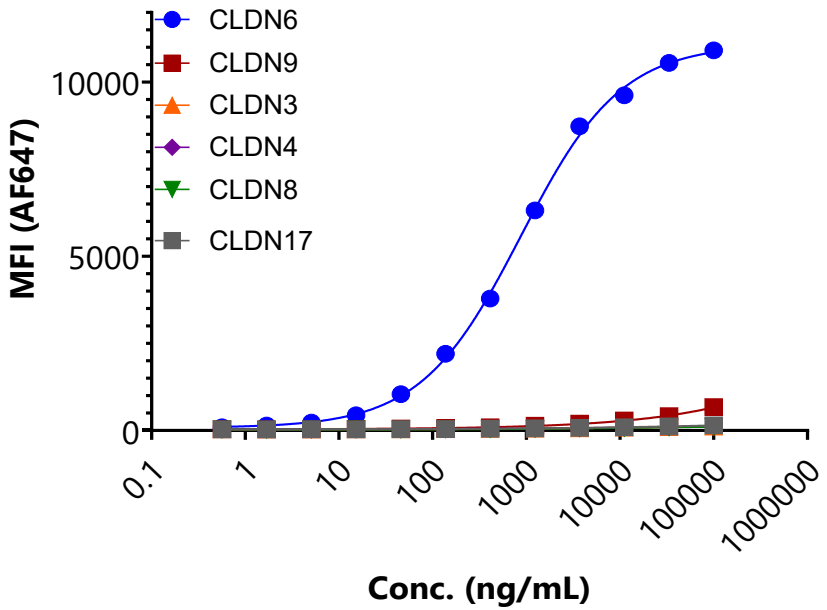
XmAb®541: CD3 T-cell Engager for Ovarian Cancer & Solid Tumors

XmAb 2+1 Design



XmAb541 (CLDN6 x CD3)

Highly selective for CLDN6 over CLDN9

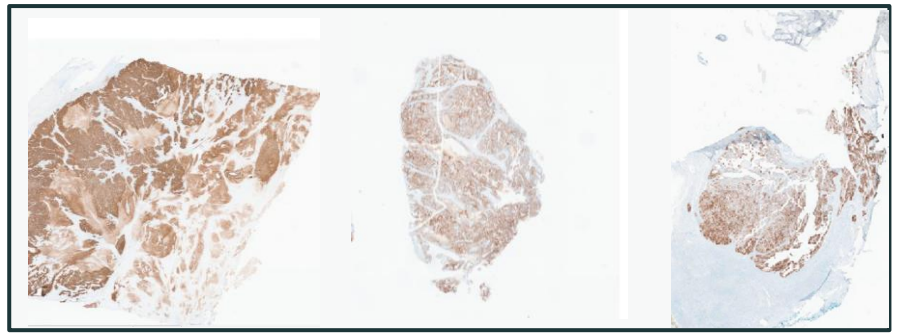


- Differential expression in cancerous tissue presents CLDN6 as an intriguing target
- CLDN family members, which are small membrane proteins, have high sequence identity, complicating antibody design
- XmAb541 engineered for CLDN6 selectivity over similar CLDN9, CLDN3 and CLDN4

Phase 1 Dose Escalation Study

- Ongoing Phase 1 study, initiated in 1H24
- Enrolling patients with ovarian, endometrial and germ cell tumors
- CLDN6 CDx pre-screening for patients with ovarian and endometrial cancers, but not required for GCT

Representative IHC from enrollment



GCT | Endometrial | Ovarian

NCT06276491

GCT germ cell tumor **MFI** mean fluorescence intensity **CDx** companion diagnostic **IHC** immunohistochemistry

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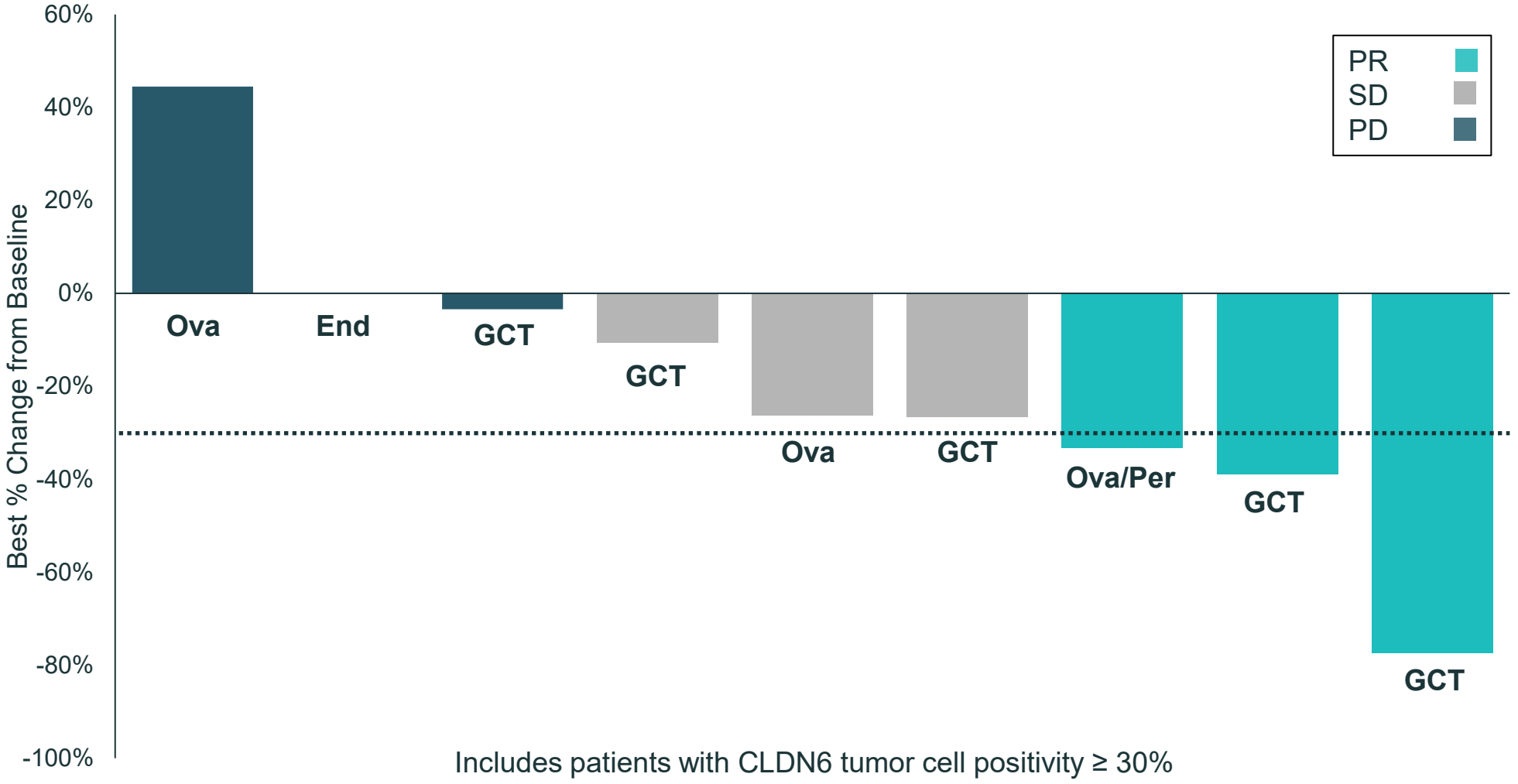
XmAb541 Best Overall Response at Most Recently Evaluated IV Dose Level



Data cut-off: October 1, 2025 **Ova** ovarian cancer **End** endometrial cancer **GCT** germ cell tumor **Per** peritoneal cancer **PR** partial response **SD** stable disease **PD** progressive disease

Market Opportunity for Xmab541 in CLDN6+ Gynecological Tumors

	Epidemiology	SoC Per Line of Therapy	Commercial Opportunity
Ovarian Cancer CLDN6 positivity: ~50-60%[1]	20k New U.S. cases/yr 1 LoT: 15k 2 LoT: 12k	Chemo ± bev ± PARPi Chemo ± bev, mirv (FRα+)	ELAHERE mirvetuximab soravtansine-gynx injection 100 mg **Total sales in 1H25:** $338 million[2] **Global TAM by 2030: ~4.5 $bn[3]**
Endometrial Cancer CLDN6 positivity: ~13-20%[1]	65k New U.S. cases/yr 1 LoT: 15k 2 LoT: 7k	Chemo + PD-1 therapies Chemo + PD-1 therapies	Jemperli (dostarlimab) Injection 500 mg **Total sales in 1H25:** $196 million[2] **Global TAM by 2030: ~4.5 $bn[3]**
Germ Cell Tumors CLDN6 positivity: ~80-90%[4]	10k New U.S. cases/yr 1 LoT: 3k 2 LoT: 1k	Platinum-based chemo Chemo ± autologous transplant	~~Approved drugs~~ **Global TAM by 2035: ~4.2 $bn[5]**

1 Xencor internal data **2** Q2 2025 Company earnings **3** GlobalData **4** Clin Cancer Res (2023) 29 (11): 2131–2143 **5** IMARC Group **LoT** line of therapy **TAM** total addressable market

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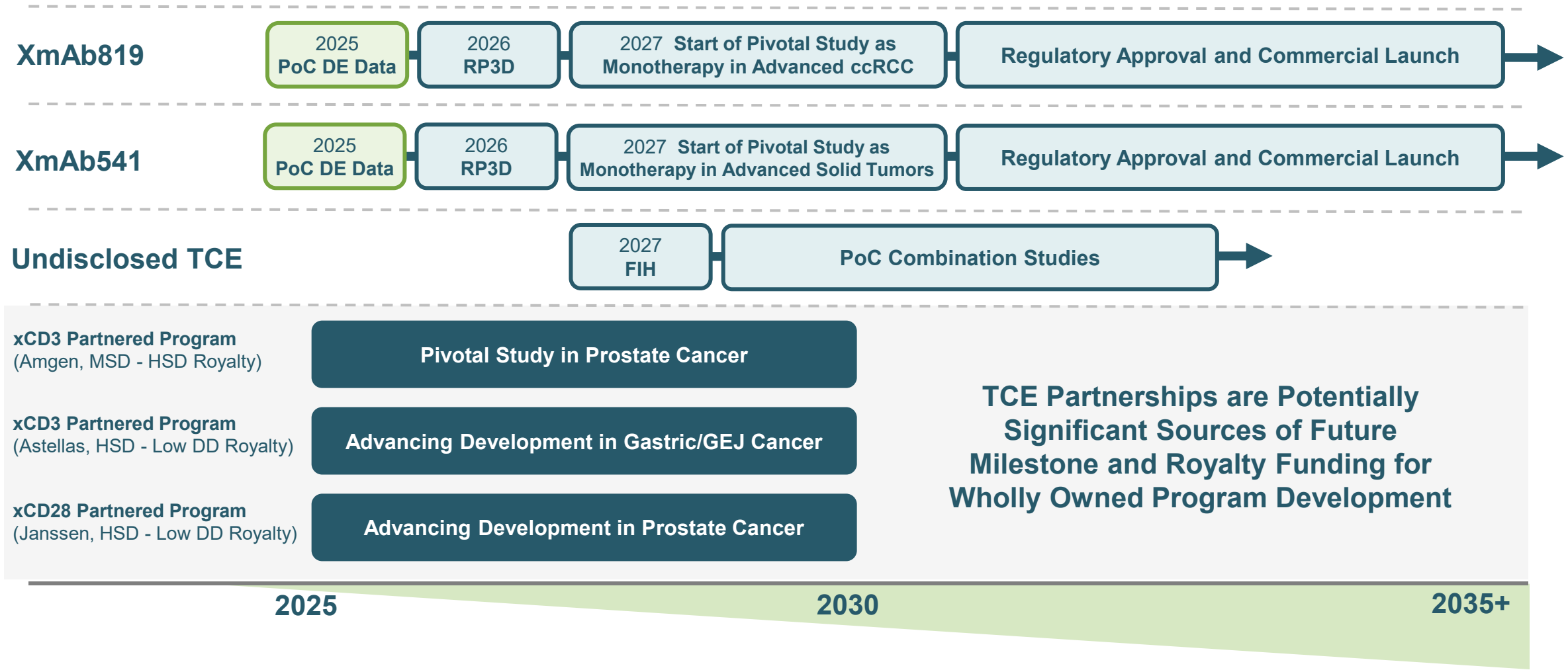
Closing Remarks

Building a Fully Integrated Oncology Company on Novel TCEs



TCE T-cell engager **PoC** Proof of concept **DE** dose escalation **RP3D** recommended Phase 3 dose **ccRCC** clear cell renal cell carcinoma
FIH first-in-human **MSD** mid-single digit **HSD** high-single digit **DD** double digit **GEJ** gastroesophageal junction

Initial Results from Ongoing Dose-Escalation Study of XmAb819 & Oncology Pipeline Update

October 24, 2025