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Our Time is Now

January 2021

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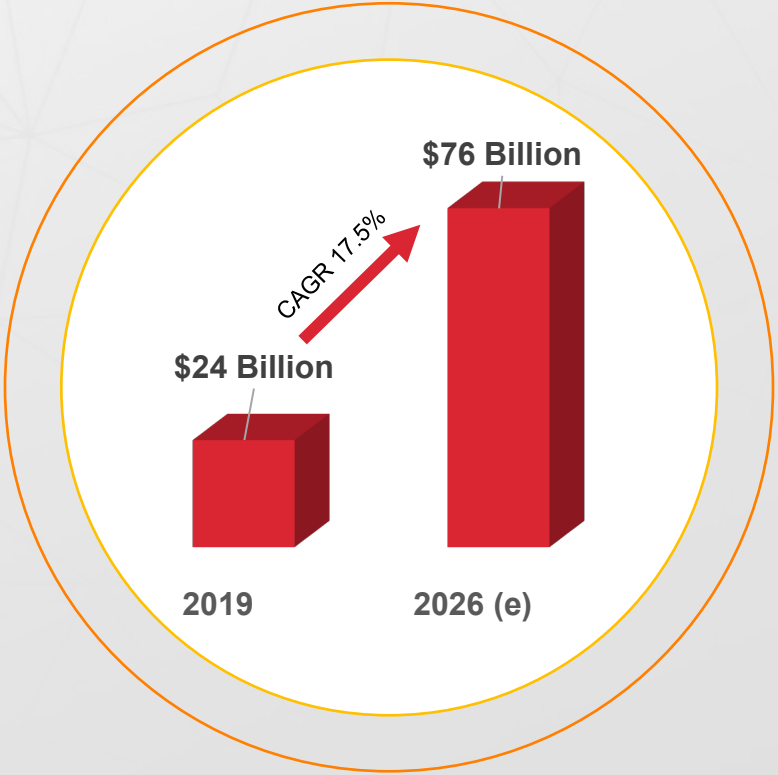
Tilsotolimod:
Injecting Innovation into Cancer Immunotherapy

Our time is now

- Significant Patient Need
- Competitive Attributes
- Advanced Melanoma
- Moving Beyond Melanoma
- Strong Exclusivity and Financial Readiness

As cancer incidence continues to rise, spending on global PD-(L)1 therapies are projected to more than triple

- **Increased diagnoses**
  - Rising incidence of cancer
  - Greater disease awareness
  - Timely detection
- **New approved uses of existing PD-(L)1 therapies**
- **New compounds**
- **Use in earlier lines of therapy**



QY Research; Global PD-1 and PD-L1 Inhibitors Industry Research Report, Growth Trends and Competitive Analysis 2020-2026

Significant unmet need remains

- Patients with advanced cancer typically have a **poor prognosis**
- As many as **87% of patients progress** due to primary or acquired resistance to anti-PD-(L)1s[1]
- If shown to be an effective therapy post anti-PD-1, **tilsotolimod could provide hope to many cancer patients**

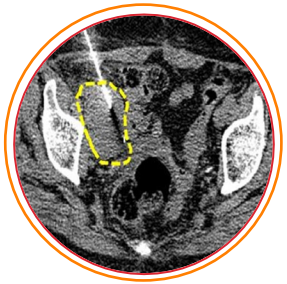
[1] Haslam and Prasad. *JAMA Network Open.* 2019;2(5):e192535.

Key Attributes of Tilsotolimod

vs other therapies following anti-PD-1

- May help overcome resistance to anti-CTLA-4s
- Encouraging safety profile
- Non-viral

- Can be administered into deep lesions or viscera



(with radiology guidance)

- Single site of injection
- No device needed
- Total treatment duration of 6 months*

* For tilsotolimod + ipilimumab combination in ILLUMINATE-301

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Tilsotolimod is the most advanced TLR9 agonist in development.

Phase 3 data is imminent

✓**Late Q1 2021**

Activates both TNFα *and* B cells

✓ TNFα → activation and proliferation of naïve and effector T cells

✓ Checkpoint inhibitors require **T-cells & B-cells** to effectively fight cancer

Purposeful Structure

✓ Potency via 2 accessible 5'-ends, which are needed for **immune activation**

✓ Avoids increased manufacturing complexity for virus-like particle encapsulation

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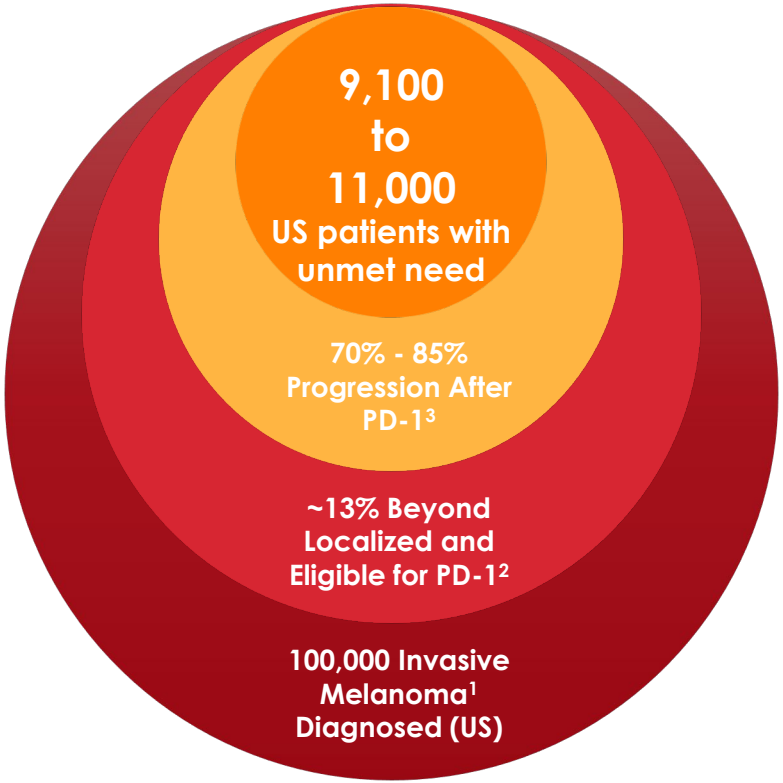
Tilsotolimod Clinical Trials

Advanced Melanoma

- Patient Need
- Illuminate 301
- Market Potential
- Next Steps

Most Melanoma Patients Progress After PD-1

This may be the result of the absence of T-cells and/or acquired immune resistance, limiting the ability of the immune system to target the tumor



1. American Cancer Society. www.cancer.org/cancer/melanoma-skin-cancer/about/key-statistics.html. Accessed January 7, 2021. **2.** Watson et al. *J. Am. Acad. Dermatol.* 2011;65(5):S6 **3.** Mooradian and Sullivan. *Cancer Network.* 2019;33(4).

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Ipilimumab alone does not seem to sufficiently address the unmet need in anti-PD-1 refractory patients.

Historical data of 321 patients suggest ipilimumab monotherapy ORR of 9.5% and DCR of 28.7%*

* ORR: Overall Response Rate; DCR: Disease Control Rate.

Weighted average of above 6 studies. There are three additional studies of n=9, n=8, n=7 respectively: Aya, et al., Future Oncol. 2016;12(23):2683-2688 (ORR=22%); Jacobsoone-Ulrich et al., Melanoma Res. 2016;26(2):153-156 (ORR=50%); Saijo, et al., Tohoku J. Exp. Med., 2019;248:37-43 (ORR=0%).

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N	ORR	DCR	Reference
97	13%	45%	Long et al (2016, Nov). Outcomes in patients treated with ipilimumab after pembrolizumab in KEYNOTE-006. Presented at the Society for Melanoma Research 2016 Congress, Boston, MA.
60	4%	16%	Fujisawa et al. Retrospective study of advanced melanoma patients treated with ipilimumab after nivolumab: Analysis of 60 Japanese patients. J. Dermatol. Sci. 2018;89(1):60-66.
47	4%	17%	Weichenthal et al. Salvage therapy after failure from anti PD-1 single agent treatment, A Study by the German ADOReg melanoma registry. J. Clin. Oncol. 2019;37:15_suppl,9505.
47	16%	42%	Zimmer et al. Ipilimumab alone or in combination with nivolumab after progression on anti PD-1 therapy in advanced melanoma. Eur. J. Cancer. 2017;75:47-55.
40	10%	18%	Bowyer et al. Efficacy and toxicity of treatment with the anti-CTLA-4 antibody ipilimumab in patients with metastatic melanoma after prior anti-PD-1 therapy. Br. J. Cancer. 2016;114(10):1084-1089.
30	7%	13%	Muto et al. Investigation of clinical factors associated with longer overall survival in advanced melanoma patients treated with sequential ipilimumab. J. Dermatology. 2019;46:498-506.

Tilsotolimod, in combination with ipilimumab, may address that unmet need

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Ipilimumab-naïve patients with anti-PD-1 refractory advanced melanoma

1:1
N ≈ 454

Arm A
- **Ipilimumab 3 mg/kg**
  Treatment Duration: 10 weeks

No Crossover

Arm B
- **Ipilimumab 3 mg/kg**
  +
- **Intratumoral tilsotolimod 8 mg**
  Treatment duration: 24 weeks

Primary endpoint family
- **ORR** by independent review per RECIST v1.1
- **OS**

Key secondary endpoints
- Durable response rate (DRR)
- Duration of response (DOR)
- Time to response
- Progression-free survival (PFS)
- PFS and OS at 1 & 2 years
- Patient-reported outcomes
- Safety

BMS is providing Idera the ipilimumab for ILLUMINATE-301 free of charge

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ILLUMINATE-301

Success factors

Accelerated Approval would be sought based on the totality of the topline data available in late Q1 2021 →

Study to continue to OS outcome

- **Statistically and clinically meaningful improvement in response rate**
  - For example: ORR of 20% in combination arm vs 10% in ipilimumab-alone arm
- **Positive supporting data**
  - Duration of response (DOR)
  - Disease control rate (DCR)
- **Encouraging safety profile**

Reasons to Believe

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Tilsotolimod Clinical Trials

Data from ILLUMINATE-204 show potential for clinically meaningful benefit

	Data from Tilsotolimod (8 mg) + Ipilimumab in ILLUMINATE-204, % (n) (n=49)[1]	Historical Data of Ipilimumab Monotherapy: (n=321)[2]
Overall Response Rate (CR or PR)	**22.4% (11)** (95% CI: 11.8-36.6%) **Median Duration of Response (DOR) of 11.4 months** (95% CI: 3.3 – NR)	9.5%
Disease Control Rate (CR, PR, or SD)	**71.4% (35)** (95% CI: 56.7-83.4%)	28.7%
Safety	**Encouraging Safety Profile**	
Median Overall Survival	**21.0 months** (95% CI: 9.8-NR)	

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1. 49 of 52 subjects had at least 1 post-baseline disease assessment
2. Weighted average from pooled post-hoc analysis of 6 studies in post-PD-1 patients. References available on Slide 10.
NR: not reached

Success in ILLUMINATE-301 could yield a significant commercial opportunity in melanoma

Peak year sales estimates[1], if approved:

US: ~$600 million

EU: ~$350 million

1. Based on current company forecast through 2037

Planning for Success

If approved, MODTYLSO (tilsotolimod) will be Idera's first commercial product

COO Dan Soland added to the team

Responsibility for Commercial & CMC

NDA & supply chain readiness well under way

Planning for rolling submission & priority review

Commercial team buildout to begin in late 2021

Total commercial team est. ~50 or fewer

Moving Beyond Melanoma

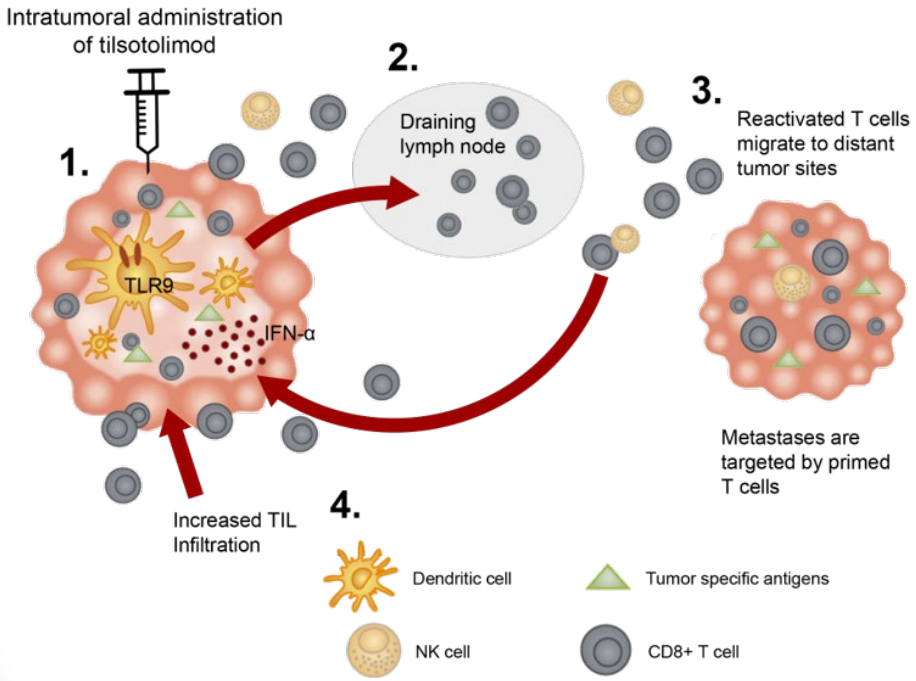
Tilsotolimod Expansion Opportunity

Tilsotolimod may contribute to better patient outcomes

Designed to stimulate the immune system.

- Binds to TLR9
- Alters the tumor microenvironment in both injected and non-injected tumors
- Supports innate and adaptive immunity
- **Results in tumor cell death**

(HAYMAKER et. al., ESMO 2020)



We believe the well-established mechanism of action may apply in many tumor types

Key evidence supporting the MOA

- Activation of Type I interferon pathway
- Maturation of intratumoral dendritic cells (DC)
- Increased immune infiltration & expansion of major T cell clones
- Tumor regression correlated to presence of Ki67+ T-cells
- Responses observed in tumors with low HLA-ABC baseline expression, which are resistant to ipilimumab alone

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Translational data from Ph 2 trial of tilsotolimod + ipilimumab in patients with anti-PD-1 refractory advanced melanoma*

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Translational data from tilsotolimod monotherapy study in multiple tumor types†

Idera pre-clinical studies

*Haymaker, ESMO 2020
†Babiker, AACR 2020

Regardless of tumor type, tilsotolimod induced rapid gene expression changes in the tumor microenvironment

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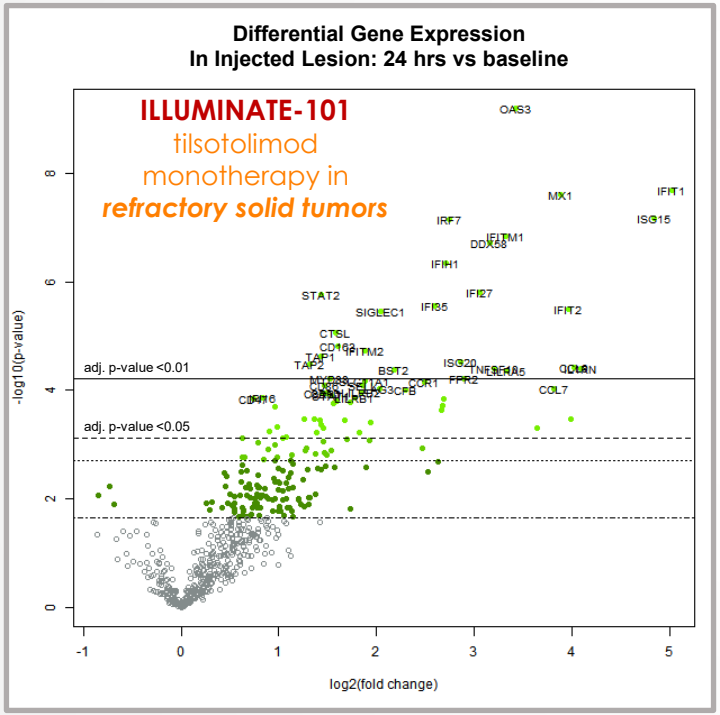
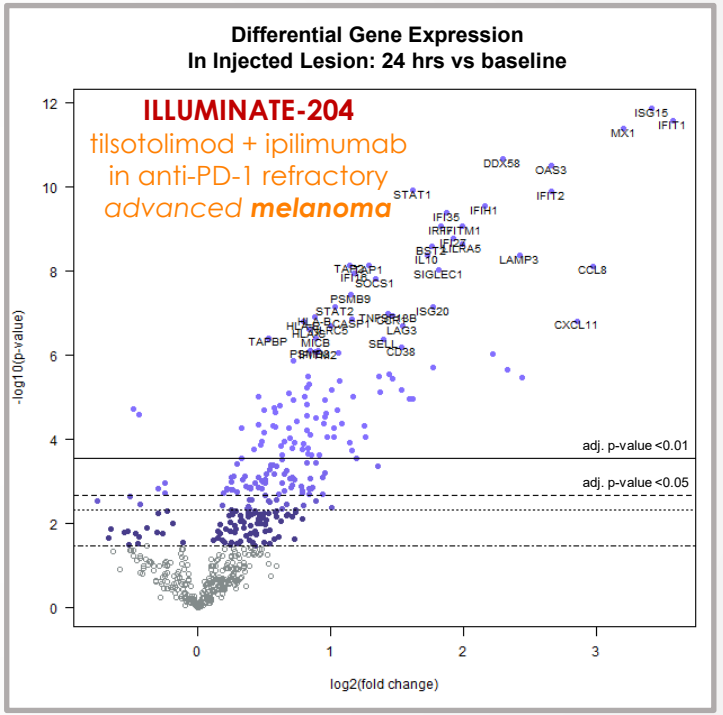
Tilsotolimod Clinical Trials





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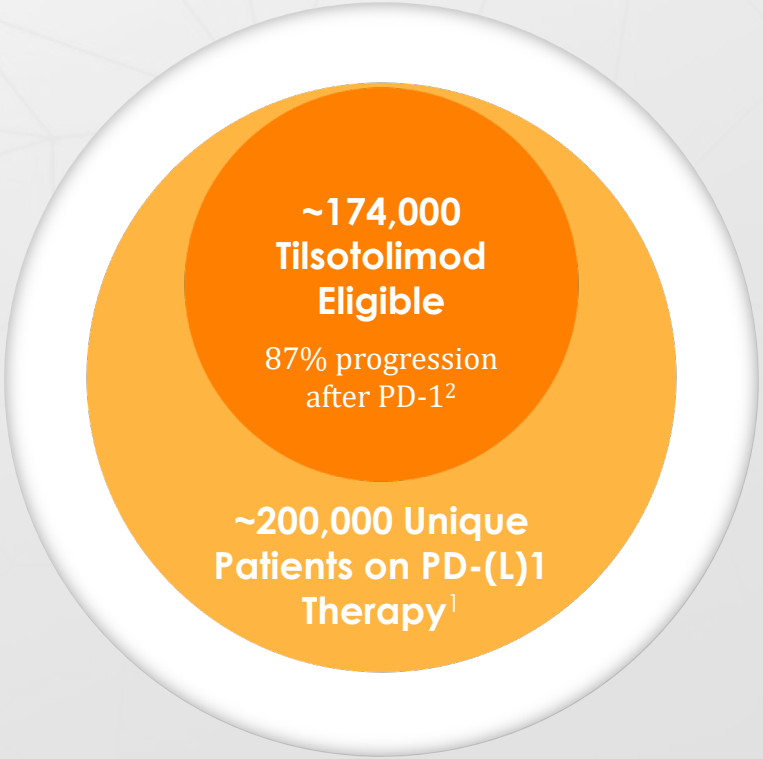
Tilsotolimod represents multi-billion-dollar potential to improve patient outcomes following PD-(L)1 therapy

Use in emerging I/O-addressable tumors

Moderate response to cornerstone anti-PD-1

Goal to increase number of approved settings



Use with "cold" tumors not addressable with current I/O

Significant opportunity in tumors with:

Low mutation load

Low dendritic cell infiltration

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[1] IQVIA Institute. Global Oncology Trends 2019. Parsippany, NJ.
[2] Haslam and Prasad. *JAMA Network Open.* 2019;2(5):e192535.

ILLUMINATE-206 Multicohort Protocol Design

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Cohorts for each tumor type & combination

First indication:
MSS-CRC

Highly immunosuppressive with no approved I/O options

High Unmet Need

Of total CRC cases, **MSS represents 80-85%** (& a higher proportion of deaths)

~140,000 new MSS-CRC cases with ~50,000 deaths per year

Significant Commercial Potential

Potential US peak year sales for tilsotolimod in MSS-CRC:

> $1.6B[1]

BMS is providing Idera the ipilimumab and nivolumab for ILLUMINATE-206 free of charge

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[1]Based on current company forecast through 2037

Next Data Coming in 3Q

Tilsotolimod + nivolumab + ipilimumab in MSS-CRC

- **Encouraged by initial safety profile along with 1 SD per RECIST v1.1**
  - 6 of the progressing patients had stability or reduction in size of injected lesions
  - 6 had stability or reduction in overall size of non-injected lesions
- **Enrolling an additional 10 patients with changes aimed at improving outcomes**
  - Increasing frequency of ipilimumab dosing from Q8W to Q3W
  - Limiting the number of allowed prior lines of treatment to 2 or fewer
- **Data expected Q3 2021**
  - Trial may expand further pending outcomes

Clinical Collaboration with AbbVie

Further broadens commercial potential via other combinations and tumor types

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ABBV-368 (OX-40)
+
Tilsotolimod in Patients with Recurrent or Metastatic Head & Neck Squamous Cell Carcinoma (HNSCC)

abbvie

The study will test three separate treatment arms (N = 69, 23 per arm):

- ABBV-368 plus tilsotolimod;
- ABBV-368 plus tilsotolimod and nab-paclitaxel (chemotherapy); and
- ABBV-368 plus tilsotolimod, nab-paclitaxel, and ABBV-181 (anti-PD-1 agonist).

Strong Exclusivity

Three sources of exclusivity for tilsotolimod in the U.S.

Composition of Matter Patent Exclusivity

Provides exclusivity until 2030 (estimated), inclusive of patent term extension

Method-of-Use Patent

Covers certain melanoma, CRC, & HNSCC treatments in combination with therapies targeting CTLA-4, PD-1, or PD-L1

Est. expiration in Sept. 2037

Orphan Drug Designation

Granted *"for treatment of melanoma Stages IIb to IV"* by the FDA

Financials

Capital to move tilsotolimod toward commercialization in advanced melanoma

[1] Potential future closings from current private placements at investors' discretion
[2] Based on estimated, unaudited financial results and management's operating plan as of 12/31/2020
[3] Based on potential future closings from current private placements at investors' discretion

Current shares outstanding ~38M as of 12/31/2020

Our time is now

- **Tilsotolimod Opportunity Begins in Melanoma…**
  - Phase 3 trial poised to deliver
  - Data expected late Q1 2021
- **…And is Followed by MSS-CRC**
  - Next Phase 2 data subset expected Q3
- **Financial Flexibility, Exclusivity Protections, and Organizational Readiness to Deliver**

Thank You