

NEW DIGS

# FoCUS

Financing and Reimbursement  
of Cures in the US

**Preparing the System:  
Pipeline Prediction Update**

ASGCT Policy Summit  
November 5, 2019

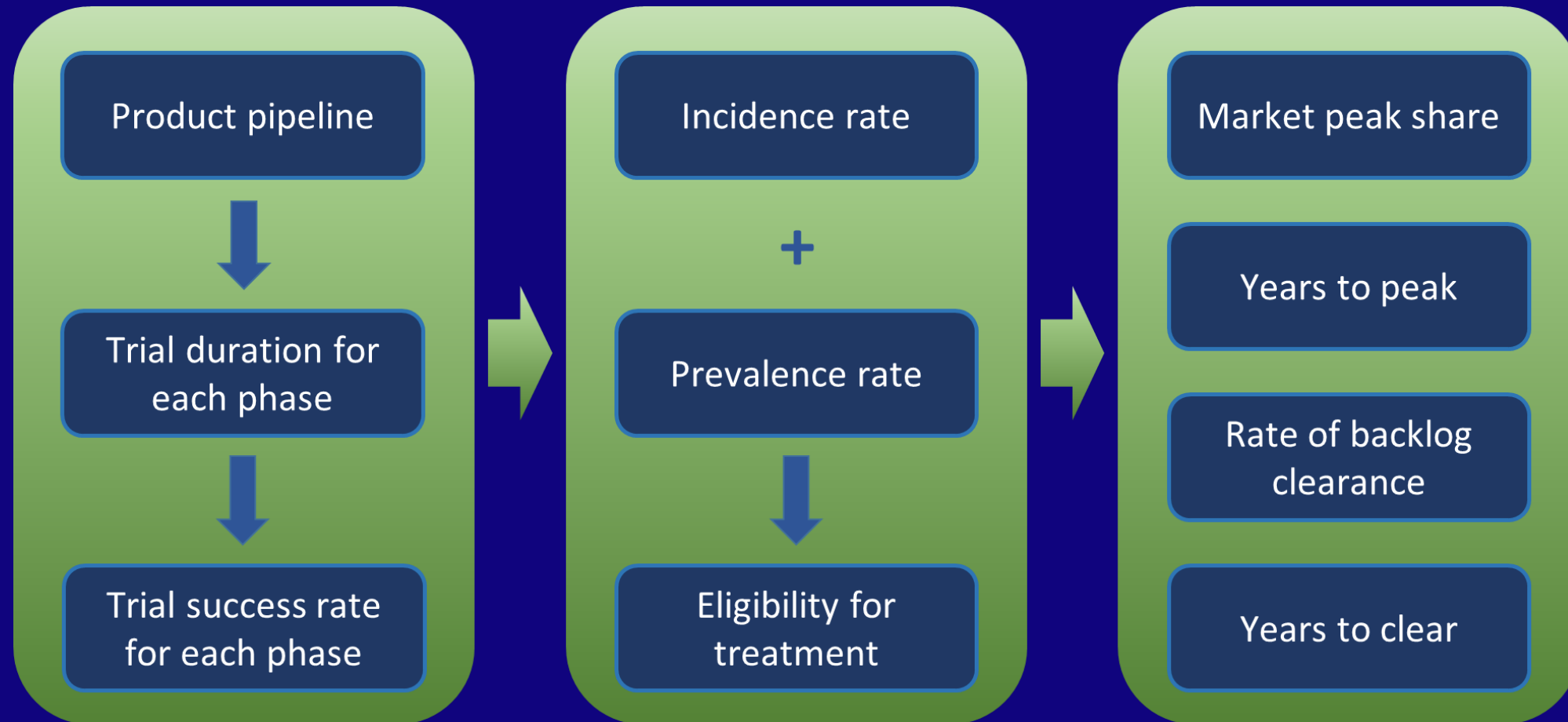
MIT CENTER FOR BIOMEDICAL INNOVATION



## Our Focus

- Durable and potentially curative therapies (*“Single shot”*)
  - Gene Therapy
    - Viral vectors - AAVs (in vivo) or Lentiviruses (ex vivo)
    - Direct gene editing - CRISPR Cas9, Zinc finger, TALEN
    - Plasmids – signaling proteins (i.e. VEGF)
  - Oncology
    - CAR-T, TCR and other related therapies
- Potential for US marketing approval
  - Registered on [clinicaltrials.gov](https://clinicaltrials.gov)
  - US based preclinical

# Pipeline Analysis Model (PAM) Overview



# Markov chain Monte Carlo Model

	Initial	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030	2031
Phase	1.5													

# Markov chain Monte Carlo Model

	Initial	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030	2031
Phase	1.5	1.5												

# Markov chain Monte Carlo Model

	Initial	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030	2031
Phase	1.5	1.5	1.5											

# Markov chain Monte Carlo Model

	Initial	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030	2031
Phase	1.5	1.5	1.5	2.0										

# Markov chain Monte Carlo Model

	Initial	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030	2031
Phase	1.5	1.5	1.5	2.0	2.0									



# Markov chain Monte Carlo Model

	Initial	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030	2031
Phase	1.5	1.5	1.5	2.0	2.0	2.0								

# Markov chain Monte Carlo Model

	Initial	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030	2031
Phase	1.5	1.5	1.5	2.0	2.0	2.0	3.0							

# Markov chain Monte Carlo Model

	Initial	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030	2031
Phase	1.5	1.5	1.5	2.0	2.0	2.0	3.0	3.0	3.0	4.0				

# Markov chain Monte Carlo Model

	Initial	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030	2031
Phase	1.5	1.5	1.5	2.0	2.0	2.0	3.0	3.0	3.0	4.0	5.0			

# Markov chain Monte Carlo Model

	Initial	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030	2031
Phase	1.5	1.5	1.5	2.0	2.0	2.0	3.0	3.0	3.0	4.0	5.0	5.0	5.0	5.0

# Markov chain Monte Carlo Model

	Initial	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030	2031
Phase	1.5	1.5	1.5	2.0	2.0	2.0	3.0	3.0	3.0	4.0	5.0	5.0	5.0	5.0

	Initial	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030	2031
Phase	1.5	1.5	-1.0	-1.0	-1.0	-1.0	-1.0	-1.0	-1.0	-1.0	-1.0	-1.0	-1.0	-1.0

# Markov chain Monte Carlo Model

	Initial	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030	2031
Phase	1.5	1.5	1.5	2.0	2.0	2.0	3.0	3.0	3.0	4.0	5.0	5.0	5.0	5.0

	Initial	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030	2031
Phase	1.5	1.5	-1.0	-1.0	-1.0	-1.0	-1.0	-1.0	-1.0	-1.0	-1.0	-1.0	-1.0	-1.0

	Initial	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030	2031
Phase	1.5	1.5	2.5	2.5	2.5	3.0	3.0	3.0	4.0	-1.0	-1.0	-1.0	-1.0	-1.0

# Markov chain Monte Carlo Model

	Initial	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030	2031
Phase	1.5	1.5	1.5	2.0	2.0	2.0	3.0	3.0	3.0	4.0	5.0	5.0	5.0	5.0

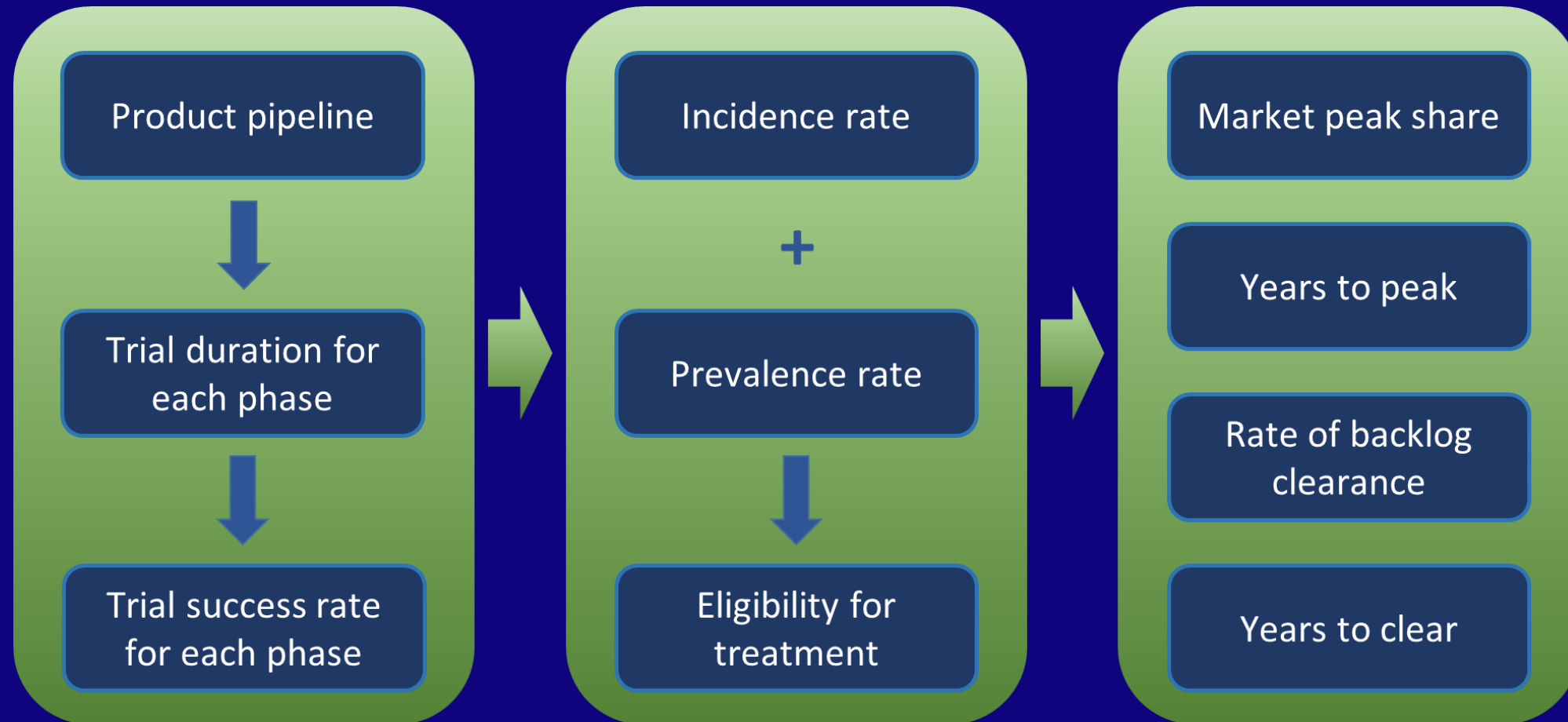
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Phase	1.5	1.5	-1.0	-1.0	-1.0	-1.0	-1.0	-1.0	-1.0	-1.0	-1.0	-1.0	-1.0	-1.0

	Initial	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030	2031
Phase	1.5	1.5	2.5	2.5	2.5	3.0	3.0	3.0	4.0	-1.0	-1.0	-1.0	-1.0	-1.0

	Initial	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030	2031
Phase	1.5	1.5	2.0	2.0	-1.0	-1.0	-1.0	-1.0	-1.0	-1.0	-1.0	-1.0	-1.0	-1.0



# Pipeline Analysis Model (PAM) Overview



# What's in the pipeline

- Oncology
  - Primarily CAR-T and TCRs – mostly autologous
  - 779 clinical trials programs (575 active)
  - 377 disease/differentiator pairs
- Differentiators
  - Typically targeted antigens
  - Viruses (HPV, EBV)
  - Other oncological proteins

# What's in the pipeline

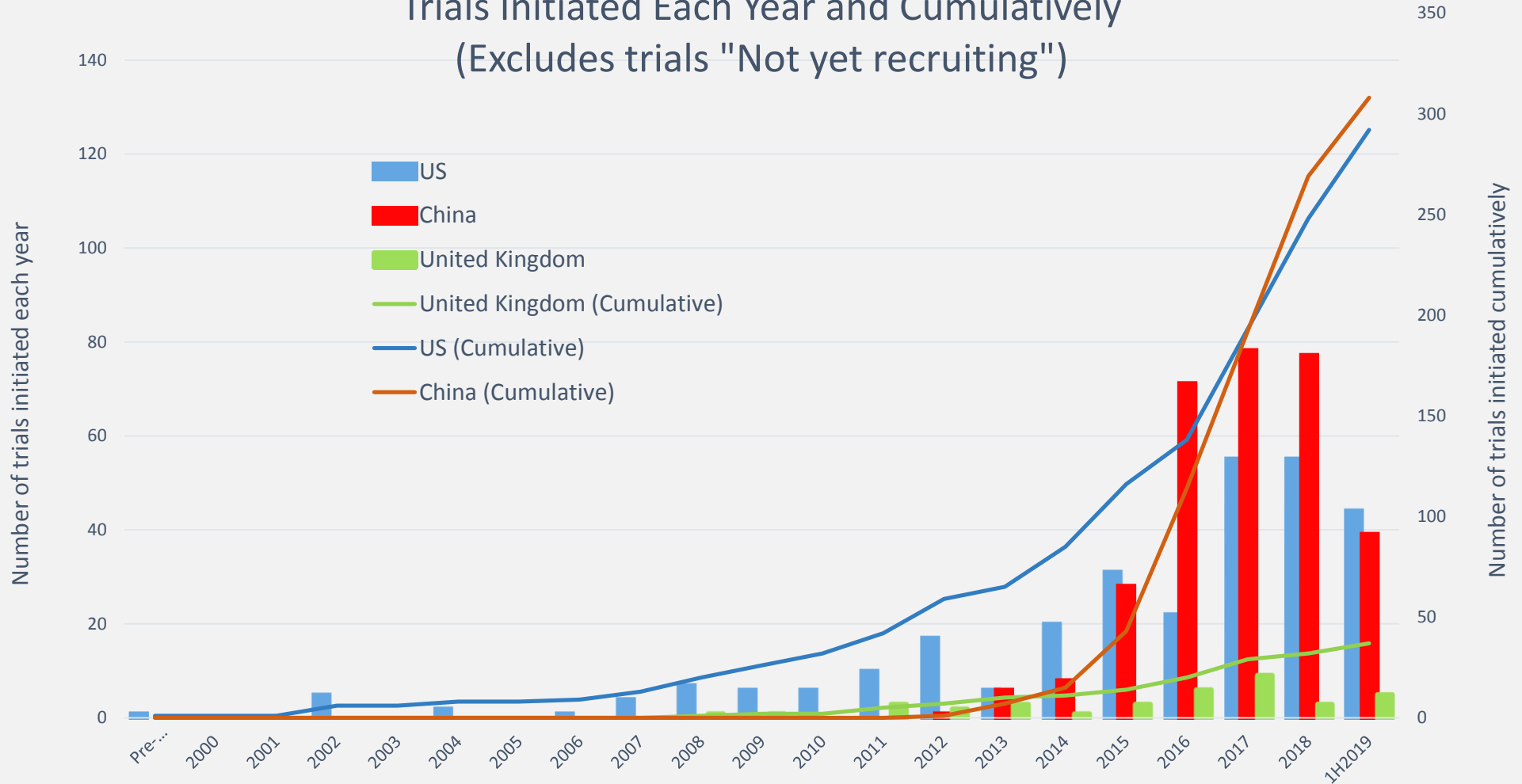
- Gene therapy
  - 316 preclinical programs - US based companies
  - 241 clinical trials programs (141 active)
  - 130 disease/differentiator pairs
- Differentiators
  - Typically specific target genes
  - Encourage production of (or suppress) a signaling protein

## Price assumptions used in the model

- **Gene therapy**
  - Ultra-Orphan \$1,500,000 (Prevalence < 10,000)
  - Orphan \$800,000 (Prevalence < 200,000)
  - Higher Prevalence \$500,000
- **Oncology**
  - CAR-T/TCR \$400,000

# Oncology

## NCT Trials by Country of Originator Trials Initiated Each Year and Cumulatively (Excludes trials "Not yet recruiting")



## Active Oncology Pipeline – 6/30/2019

	Early Phase 1	Phase 1	Phase 1 Phase 2	Phase 2	Phase 2 Phase 3	Phase 3	Total
<b>Recruiting</b>	19	272	190	32	4	1	518
<b>Active, not recruiting</b>	3	39	9	4	0	0	55
<b>Enrolling by invitation</b>	1	1	0	0	0	0	2
<b>Total</b>	23	312	199	36	4	1	575

## Success stories



ALL  
DLBCL

\$475,000



DLBCL

\$375,000

- Forecast: **40-50 additional hematological products** by 2031 addressing:
  - Acute and chronic lymphoblastic leukemias (primarily **CD19**)
  - B-cell lymphomas – making up the bulk of non-Hodgkins lymphomas (primarily **CD19**)
  - Multiple Myeloma (**BCMA**)



# CAR-T/TCR Projections

## Therapeutic Areas - Average Cumulative Approvals

	Initial	2024	2031
Cancer, hematological	3	20.3	47.9
Cancer, solid tumor	0	0.7	1.9
<b>Total</b>	<b>3</b>	<b>21.1</b>	<b>50.0</b>

Without China	Initial	2024	2031
Cancer, hematological	3	9.8	23.8
Cancer, solid tumor	0	0.4	1.1
<b>Total</b>	<b>3.0</b>	<b>10.2</b>	<b>24.9</b>

## Therapeutic Areas - Average Patients Treated Annually

	Initial	2024	2031
Cancer, hematological	9,803	23,370	38,661
Cancer, solid tumor	0	2,286	8,530
<b>Total</b>	<b>9,803</b>	<b>25,657</b>	<b>47,195</b>

Without China	Initial	2024	2031
Cancer, hematological	9,803	17,000	30,104
Cancer, solid tumor	0	446	2,530
<b>Total</b>	<b>9,803</b>	<b>17,446</b>	<b>32,634</b>

## CAR-T/TCR Reimbursement breakdown

### Therapeutic Areas - Average Annual Therapeutic Reimbursement (\$ Millions)

	Initial	2024	2031
Cancer, hematological	3,921	9,348	15,464
Cancer, solid tumor	0	915	3,412
<b>Total</b>	<b>3,921</b>	<b>10,263</b>	<b>18,881</b>

Without China	Initial	2024	2031
Cancer, hematological	3,921	6,800	12,042
Cancer, solid tumor	0	179	1,012
<b>Total</b>	<b>3,921</b>	<b>6,978</b>	<b>13,054</b>

### Reimbursement – Payer breakdown (\$Millions)

	Initial	2024	2031
Medicaid	241	388	676
Medicare	2,522	7,270	12,938
All other	1,157	2,605	5,267
<b>Total</b>	<b>3,921</b>	<b>10,263</b>	<b>18,881</b>

Without China	Initial	2024	2031
Medicaid	241	285	480
Medicare	2,522	5,197	9,211
All other	1,157	1,497	3,364
<b>Total</b>	<b>3,921</b>	<b>6,978</b>	<b>13,054</b>

# Gene Therapy

## Active Gene Therapy Pipeline – 6/30/2019

	Early Phase 1	Phase 1	Phase 1 Phase 2	Phase 2	Phase 2 Phase 3	Phase 3	Total
<b>Recruiting</b>	0	14	70	8	4	7	<b>103</b>
<b>Active, not recruiting</b>	0	14	18	1	2	1	<b>36</b>
<b>Enrolling by invitation</b>	0	2	0	0	0	0	<b>2</b>
	<b>0</b>	<b>30</b>	<b>88</b>	<b>9</b>	<b>6</b>	<b>8</b>	<b>141</b>
<b>Preclinical</b>							<b>316</b>

## Success Stories



**\$850,000**

Retinitis Pigmentosa  
& Leber's Congenital  
Amaurosis (RPE65)

"RPE65" incidence: ~60  
"RPE65" prevalence: ~1100

Total incidence: ~2,000  
Total prevalence: ~90,000+

**Not fatal**  
**No alternative treatment**



**\$2,100,000**

Spinal Muscular  
Atrophy

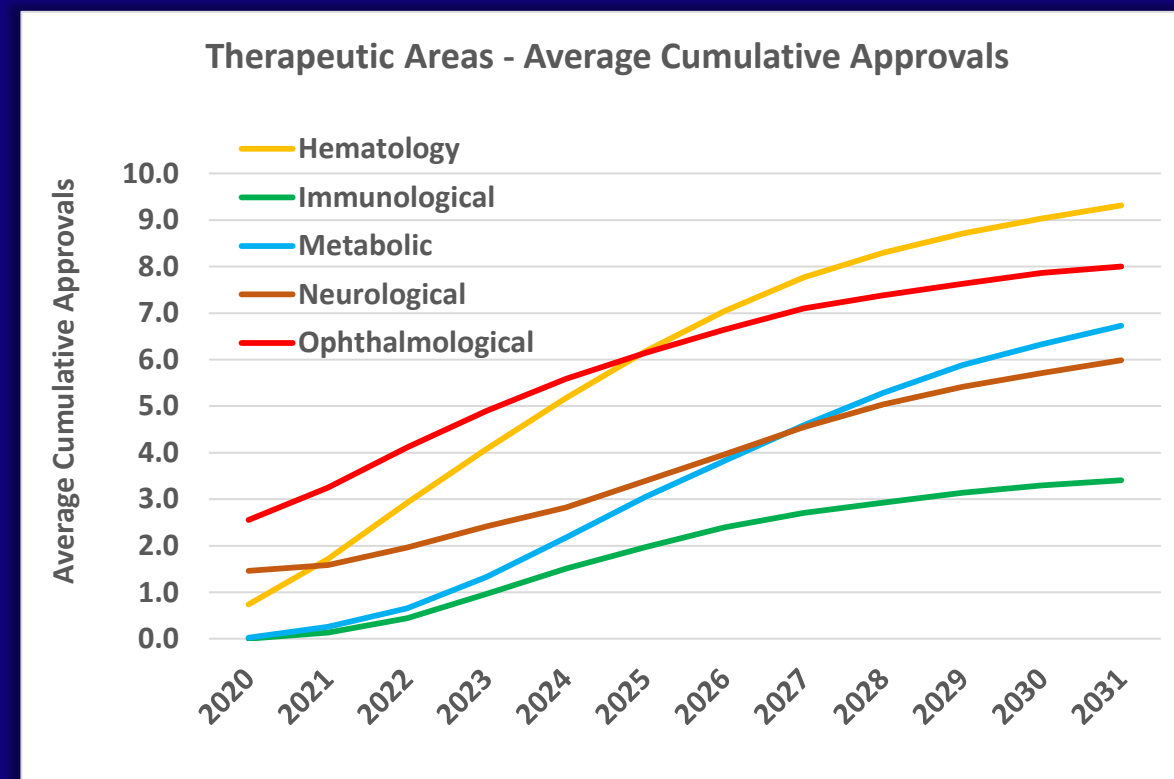
Label incidence: ~310  
Label prevalence: ~425

Total incidence: ~425  
Total prevalence: ~5,300

**Fatal**  
**Alternative treatment**

## Therapeutic Areas - Average Cumulative Approvals

	Initial	2024	2031
Cardiovascular	0	0.2	0.5
Hematology	0	5.2	9.3
Immunological	0	1.5	3.4
Infectious Disease	0	0.1	0.3
Metabolic	0	2.2	6.7
Musculoskeletal	0	1.1	2.7
Neurological	1	2.8	6.0
Ophthalmological	2	5.6	8.0
Other	0	1.2	2.9
<b>Total</b>	<b>3.0</b>	<b>19.8</b>	<b>39.9</b>



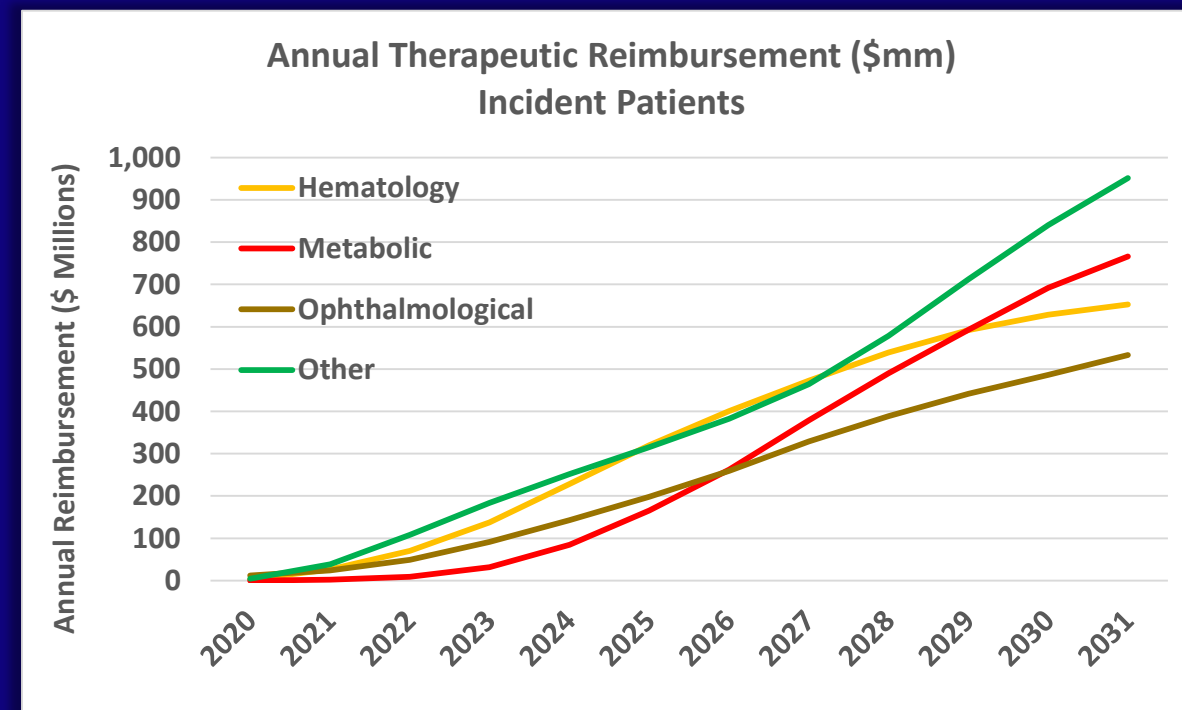
## Therapeutic Areas - Average Number of Patients Treated Annually

Incident	Initial	2024	2031
Cardiovascular	0	18	281
Hematology	0	329	938
Immunological	0	19	109
Infectious Disease	0	4	118
Metabolic	0	65	701
Musculoskeletal	0	109	298
Neurological	1	397	2,966
Ophthalmological	17	155	749
Other	0	464	1,024
<b>Total</b>	<b>18</b>	<b>1,560</b>	<b>7,185</b>

Prevalent	Initial	2024	2031
Cardiovascular	0	9	18
Hematology	0	2,301	902
Immunological	0	31	54
Infectious Disease	0	29	16
Metabolic	0	330	487
Musculoskeletal	0	327	98
Neurological	0	278	689
Ophthalmological	0	1,235	357
Other	0	232	103
<b>Total</b>	<b>0</b>	<b>4,774</b>	<b>2,724</b>

## Average Therapeutic Reimbursement - Incidence - (\$ Millions)

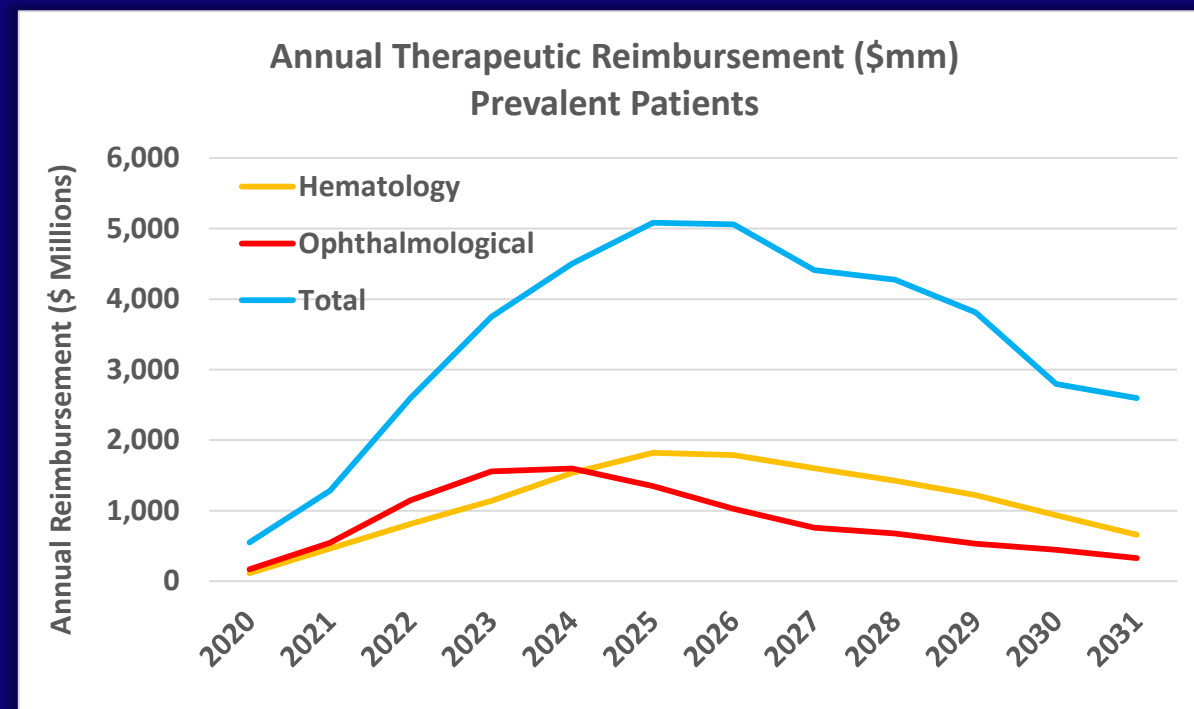
	Initial	2024	2031
Cardiovascular	0	10	145
Hematology	0	228	653
Immunological	0	29	163
Infectious Disease	0	2	63
Metabolic	0	84	766
Musculoskeletal	0	88	300
Neurological	2	389	2,210
Ophthalmological	13	143	533
Other	0	252	951
<b>Total</b>	<b>15</b>	<b>1,225</b>	<b>5,784</b>





## Average Therapeutic Reimbursement - Prevalence - (\$ Millions)

	Initial	2024	2031
Cardiovascular	0	5	11
Hematology	0	1,535	658
Immunological	0	47	81
Infectious Disease	0	15	8
Metabolic	0	411	487
Musculoskeletal	0	435	145
Neurological	0	247	741
Ophthalmological	0	1,597	326
Other	0	211	139
<b>Total</b>	<b>0</b>	<b>4,503</b>	<b>2,595</b>



## Reimbursement Breakdown (\$ millions)

### Gene Therapy

	Initial	2024	2031
Medicaid	8	2,693	2,237
Medicare	0	839	3,111
All Other	7	2,195	3,032
<b>Total</b>	<b>15</b>	<b>5,728</b>	<b>8,379</b>

### Gene Therapy and Oncology

	Initial	2024	2031
Medicaid	249	3,081	2,913
Medicare	2,522	8,109	16,049
All Other	1,164	4,800	8,299
<b>Total</b>	<b>3,935</b>	<b>15,991</b>	<b>27,260</b>

# Recap

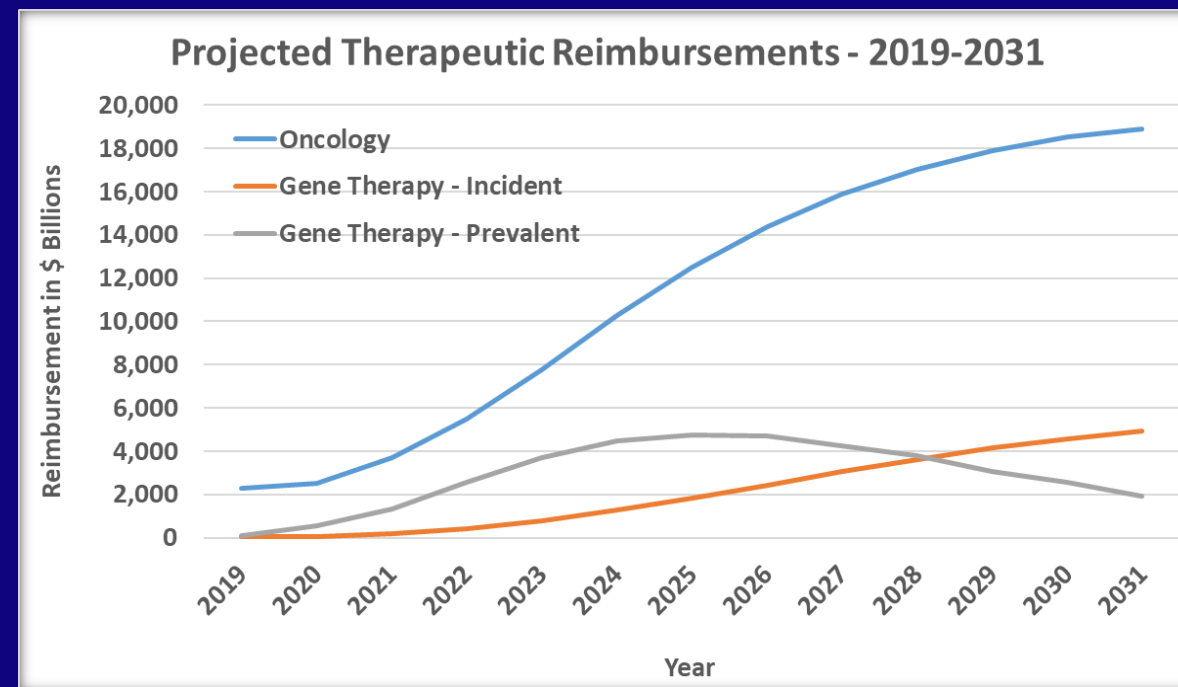
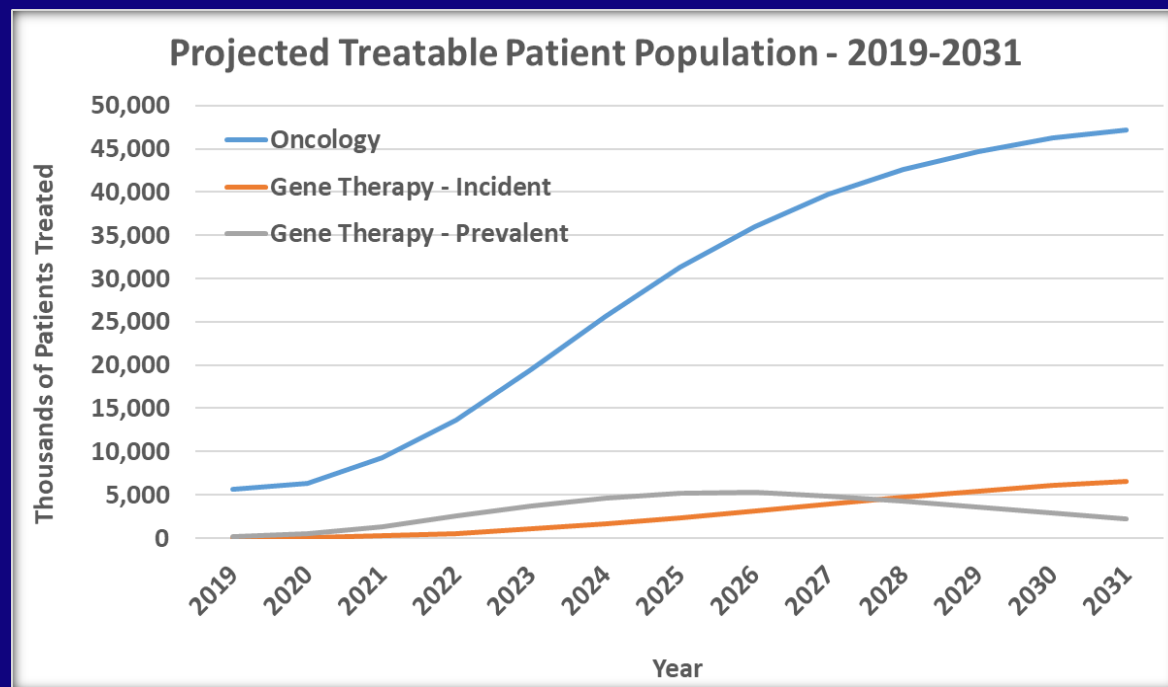
**70-90** new drug approvals by 2031

**410,000-550,000** patients treated by 2031

- 350,000-450,000 in oncology (40,000-50,000 in 2031)
- 60,000-100,000 in gene therapy (6,000-11,000 in 2031)

**\$20-30Bn** total reimbursement in 2031

- \$15-21Bn for oncological treatments
- \$5-9Bn for gene therapies



Thank You