CAR-T Reimbursement in the US

Challenges and an Assessment of Potential Solutions

groupH White Paper / Webinar

March 27th, 2019

Today's agenda

- **Introductions**
- **Background / context**
- **Current reimbursement environment**
- **Stakeholders' needs**
  - Framework to assess reimbursement proposals
- **Short-term reimbursement**
- **Short-term reimbursement proposals**
  - Medicare (2019)
  - Commercial
- **Mid-term reimbursement proposals**
- **Long-term reimbursement proposals (high-level only)**
- **Next steps discussion**

Context

- This is research was conducted as a White Paper, as groupH's own research
- It is intended as a landscape overview – a 'starting point' for future deep-dives into product-specific issues that will need further research

Introductions

groupH – the facts

Corporate

- Founded 2005
- Focus on commercial decision making during product development
- European business, with ‘headquarters’ in London
- US business, with ‘headquarters’ in San Francisco
- Virtual set-up

Team

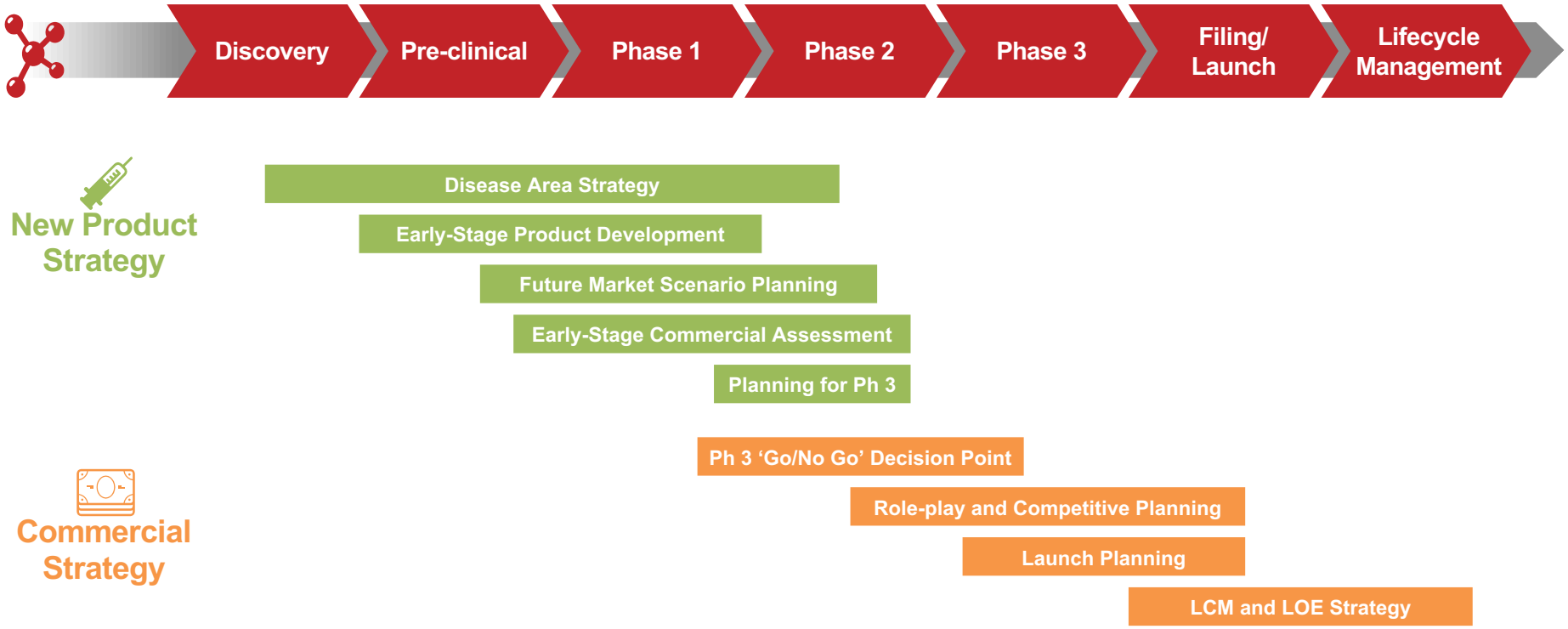
- Highly experienced senior team, extensive market knowledge
- >40 consultants and specialists spread across East Coast US, West Coast US, 5 major EU countries, BRIC and other markets
- Agile team structure enables us to deliver maximum impact within budget and time constraints

Mission

- Our Industry experience means that our deliverables meet your project needs and are ready for you to use with your key internal stakeholders
- We delight in acting as thought partners who can support our clients in making decisions that will drive their organization’s growth and success
- Actionable insights to inform commercial and clinical planning for new product development

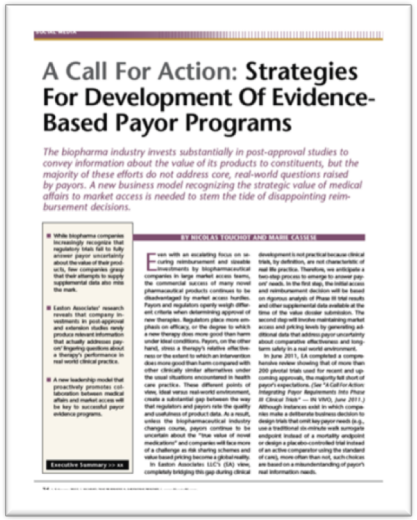
Proprietary and Confidential

groupH specializes in commercial strategy across the development pipeline



groupH Market Access practice understands the importance of building Payer's perspectives into early- and mid-stage development

Building the value story during development

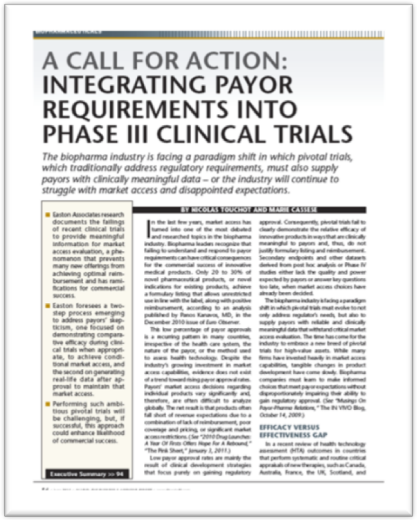


A Call For Action: Strategies For Development Of Evidence-Based Payor Programs

The biopharma industry invests substantially in post-approval studies to convey information about the value of its products to constituents, but the majority of these efforts do not address core, real-world questions raised by payors. A new business model recognizing the strategic value of medical affairs to market access is needed to stem the tide of disappointing reimbursement decisions.

In Vivo
June 2011

Integrating payer requirements into Ph 3 trials

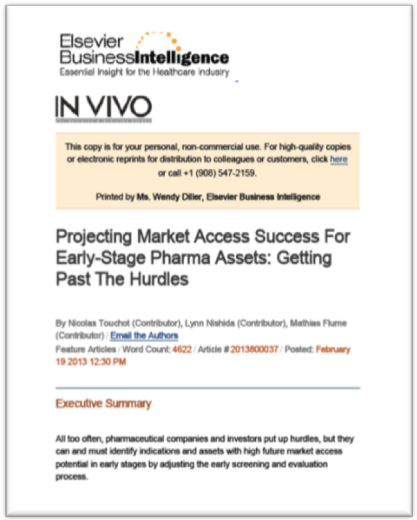


A CALL FOR ACTION: INTEGRATING PAYOR REQUIREMENTS INTO PHASE III CLINICAL TRIALS

The biopharma industry is facing a paradigm shift in which pivotal trials, which traditionally address regulatory requirements, must also supply payors with clinically meaningful data – or the industry will continue to struggle with market access and disappointed expectations.

In Vivo
February 2012

Market success for early-stage products



Elsevier BusinessIntelligence
Essential Insight for the Healthcare Industry

IN VIVO

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Projecting Market Access Success For Early-Stage Pharma Assets: Getting Past The Hurdles

By Nicolas Touchot (Contributor), Lynn Nishida (Contributor), Mathias Flume (Contributor) | Email the Authors

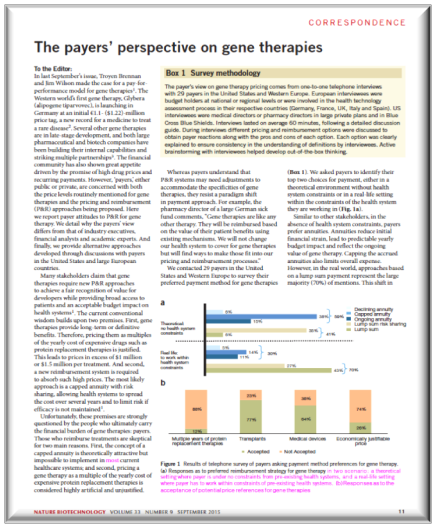
Feature Articles | Word Count: 4622 | Article #2013800037 | Posted: February 19 2013 12:30 PM

Executive Summary

All too often, pharmaceutical companies and investors put up hurdles, but they can and must identify indications and assets with high future market access potential in early stages by adjusting the early screening and evaluation process.

In Vivo
February 2013

Payer's perspectives on gene therapies



CORRESPONDENCE

The payers' perspective on gene therapies

To the Editor:

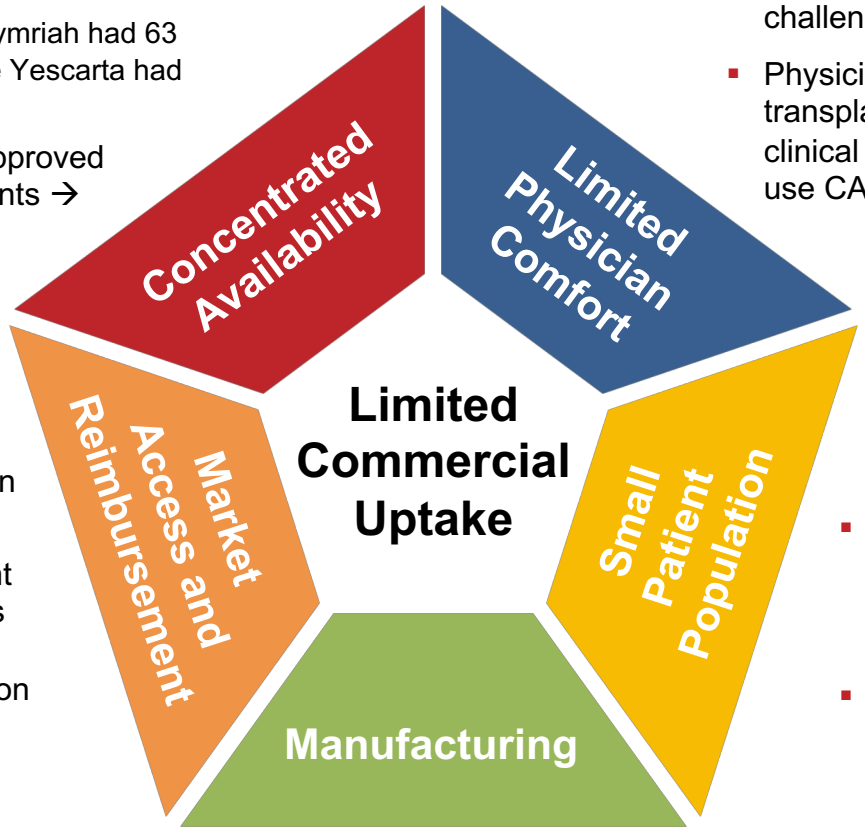
Box 1 Survey methodology

Nature Biotechnology
September 2015

There are multiple factors limiting current CAR-T commercial success – market access and reimbursement is one of them

- CAR-Ts only used in centers certified by the manufacturer
  - As of Sept 31st 2018 Kymriah had 63 approved centers while Yescarta had 64
- To date, only half of the approved centers have treated patients → administration had been concentrated

- Unlike traditional small molecules or biologics, CAR-T therapy is challenging to administer
- Physicians outside of stem cell transplant centers with an ICU or clinical trial sites more reluctant to use CAR-Ts



- High product acquisition cost puts financial burden on hospitals
- Uncertain reimbursement levels from public payers puts financial risk, and potentially large losses, on hospitals

- CAR-Ts are approved for use in DLBCL and pediatric ALL – both are orphan indications
- Furthermore, CAR-Ts are currently approved for use in later lines of therapy, further reducing the patient potential

- Last year, Novartis disclosed that they were having manufacturing difficulties with Kymriah

Source: groupH research and analysis

Today, we will focus on market access and reimbursement only

- CAR-Ts only used in centers certified by the manufacturer
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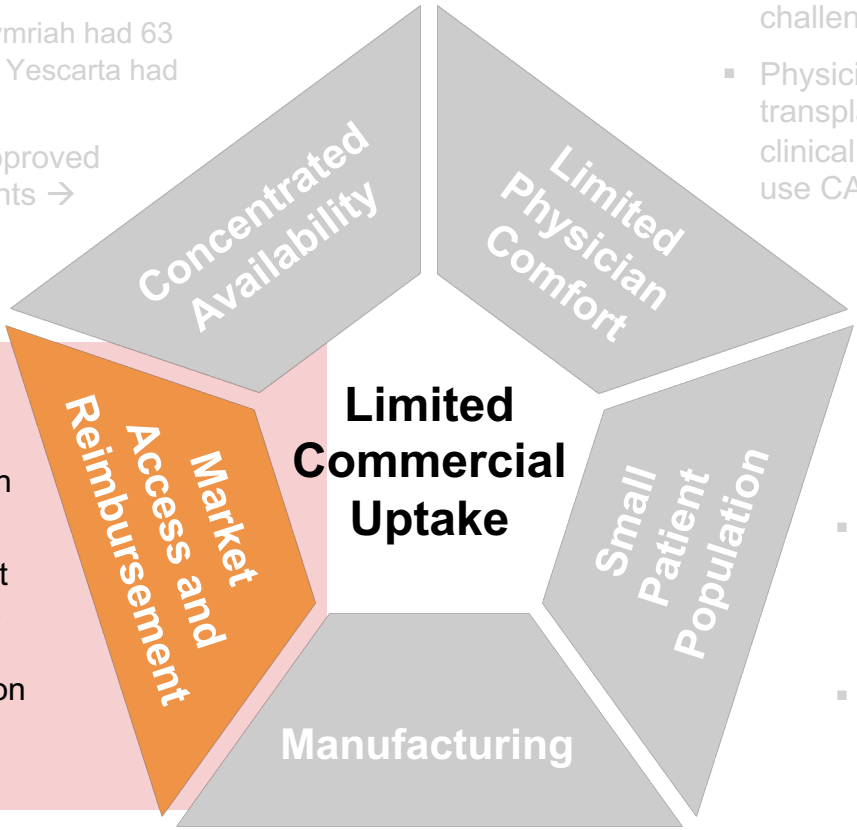

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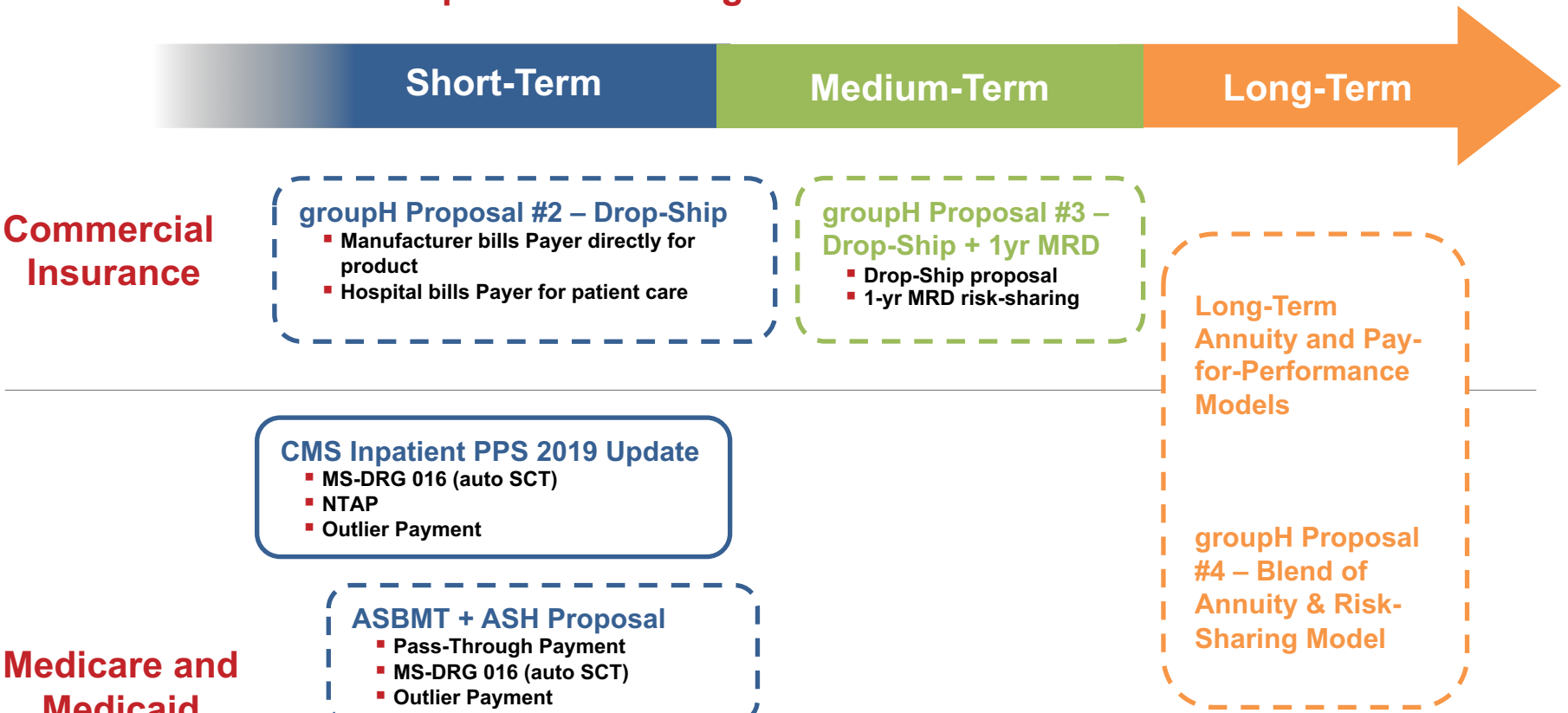
- Last year, Novartis disclosed that they were having manufacturing difficulties with Kymriah

Source: groupH research and analysis

We will review a series of step-wise proposed changes to CAR-T reimbursement, and make our own proposals, to help alleviate current problems

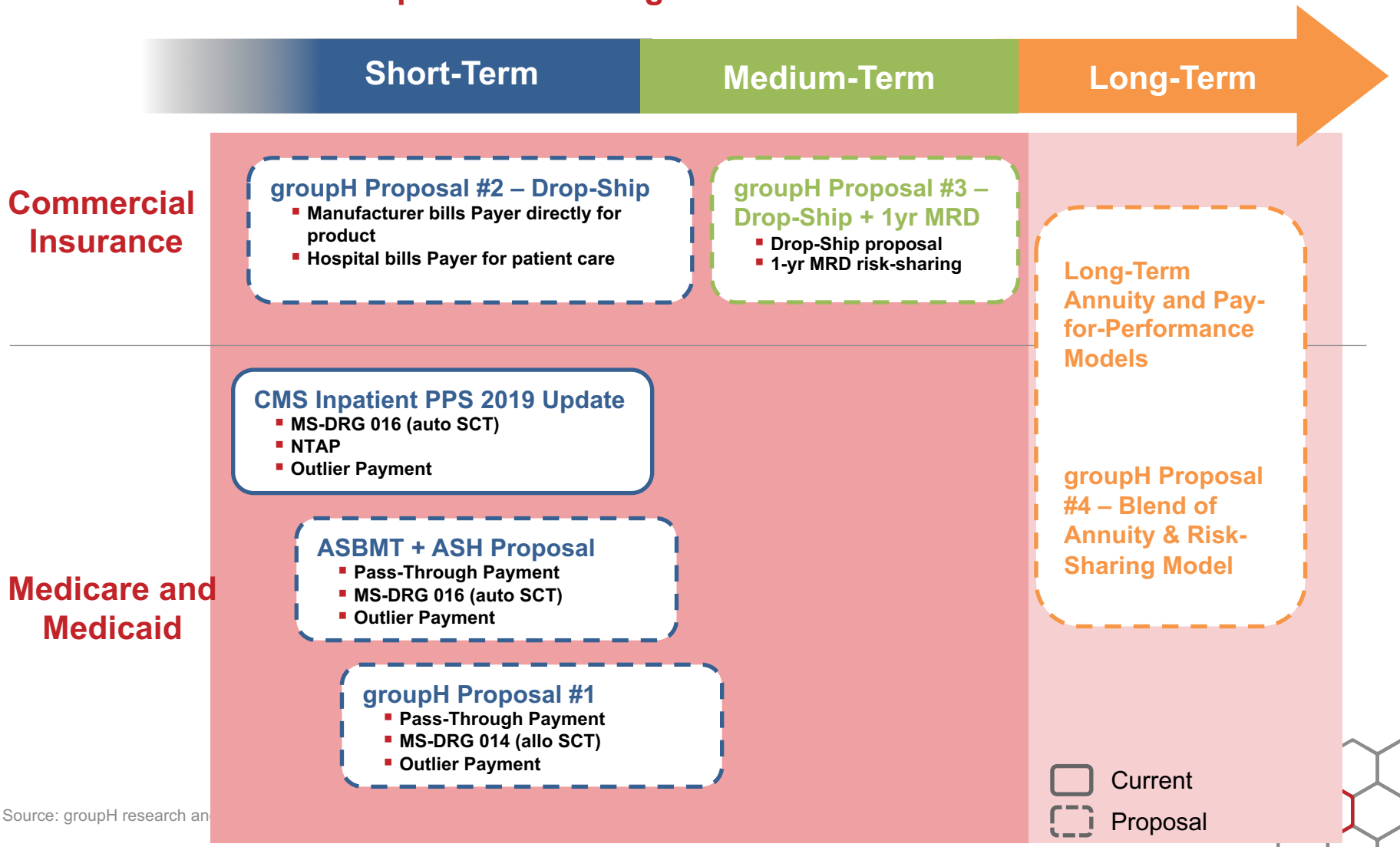
Proposals for Changes to CAR-T Reimbursement



Source: groupH research and analysis

The focus of the analysis is on improving reimbursement in the short-term and med-term, with less focus on the long-term options

Proposals for Changes to CAR-T Reimbursement



Source: groupH research an

Our research included extensive secondary research and the following primary research:

Hypothesis Development
1-hr web-assisted structured telephone discussions

Stakeholder	Sample Size	Criteria	Total Covered Lives
 **Payers**	n=4	▪ Pharmacy / Medical Directors ▪ Voting member of the formulary/P&T committee ▪ Played an active role in the coverage and reimbursement decisions for CAR-Ts ▪ CAR-T therapies covered by ≥1 book of business ▪ Good level of knowledge of CAR-T reimbursement at organization ▪ Good level of knowledge of the hospital payment mechanisms	▪ Mix of national and regional payers ▪ Commercial: 60,000,000 ▪ Medicare Advantage: 13,200,000 ▪ Managed Medicaid: 1,650,000
 **Hospital P&T Pharmacists**	n=2	▪ Voting member of the formulary/P&T committee ▪ Responsibility for leading formulary inclusion assessments for new hematology-oncology treatments ▪ Institution provides CAR-T therapy ▪ Good level of knowledge of CAR-T reimbursement at institution ▪ Good level of knowledge of the hospital payment mechanisms	N/A
 **Hospital VPs of Finance**	n=2	▪ Institution provides CAR-T therapy ▪ Good level of knowledge of CAR-T reimbursement at institution ▪ Good level of knowledge of the hospital payment mechanisms	N/A

Hypothesis Refinement
30-mins web-assisted structured telephone discussions

Stakeholder	Sample Size
 **Payers**	n=2
 **Hospital P&T Pharmacists**	n=0
 **Hospital VPs of Finance**	n=1

We did not speak with: CMS, Manufacturers (Novartis, Gilead, etc)

Executive Summary

Summary: current reimbursement

Current reimbursement differs significantly by payer type

- **Commercial:** good coverage with few restrictions beyond the product label → net positive financial outcome for hospitals providing CAR-T therapy
- **Medicare:** coverage differs significantly by setting:
  - Outpatient: ASP +6%
  - Inpatient: CMS update for PPS inpatient for 2019 allows an MS-DRG 16 payment, plus NTAP, and possible Outlier Payment
    - However, hospitals need to mark-up the CAR-T price significantly in order to achieve the max NTAP payment, but many hospitals may not know to do this
    - This is a significant improvement for providers over 2018 coverage, but still leaves hospitals with a significant shortfall on the product acquisition cost
- **Medicaid:** until NCA, coverage differs by state

Risk-sharing

- Novartis's risk-sharing approach for Kymriah in ALL is at an early stage – it is being slowly rolled out with providers and has been adopted by MassHealth Medicaid

As a result…

- Inadequate reimbursement coverage for Medicare beneficiaries means that leading hospitals with financial resources are subsidizing treatments, while others are forced to be selective in which patients they treat

Conclusion

- Reimbursement reform is imperative if CAR-T therapy is going to be is going to live up to its exciting promise

CMS Feb 15th 2019 update

- Medicare will provide CAR-T coverage with evidence development (CED); reimbursement levels not improved
- The CED could prove to be too burdensome for some providers
- The CED gives providers a legal route to opt-out of providing CAR-Ts to Medicare patients

Source: groupH research and analysis

Summary: proposals for improving reimbursement in the short-term and medium-term

	Proposals	Assessment
Medicare	**ASBMT + ASH proposal** ▪ Establish a **Pass-Through Payment** for the cost of CAR-T cells ▪ **Use MS-DRG 016 (auto SCT)** with its current **Outlier Policy** to cover some of the cost of care	▪ Allows for drug cost recovery ▪ Leaves a shortfall on the cost of care (since fewer auto SCT patients experience adverse events that require admission to the ICU than CAR-Ts) ▪ Does not include any risk-sharing
Medicare	**groupH Proposal #1** ▪ Establish a **Pass-Through Payment** for the cost of CAR-T cells ▪ Use **MS-DRG 014 (allo SCT)** rather than DRG 16 (auto SCT), with its current **Outlier Policy**	▪ Allows for drug cost recovery ▪ Further minimizes hospital losses, due to higher rate of MS-DRG 14 ▪ However, use of an allo SCT DRG is less matched to CAR-T procedure (auto) ▪ Does not include any risk-sharing
Commercial	**groupH proposal #2** ▪ **Drop-Ship Model:** payers reimburse manufacturers directly	▪ Hospital financial risk is minimized, since it does not pay the CAR-T acquisition cost ▪ Reduces the impact on hospitals' working capital ▪ However, hospitals not able to make a profit on CAR-T product ▪ Gives payers stronger buying power and ability to negotiate price directly with manufacturers ▪ Similar to approach used by high cost gene therapies (Luxturna & Spiraza)
Commercial	**groupH proposal #3** ▪ **Drop-Ship Model + 1-yr outcomes assessment**	▪ Achievable model that improves Drop-Ship to address payer long-term value concerns

Source: groupH research and analysis

Background

Introduction – considerable scientific progress and investment is being made with CAR-T therapies

"With hundreds of ongoing clinical trials and an unprecedented wave of new companies entering the field, chimeric antigen receptor (CAR) T-cell therapy represents one of the most important therapeutic and technological developments in the treatment of Leukemia and Lymphoma in years.

Landmark approvals, multi-billion dollar acquisitions, and treatment costs approaching half-a-million dollars have captivated investor imaginations, resulting in billions of dollars in capital trading hands to support research and development for CAR-T."

– Bill Koski, Seeking Alpha (Aug 2018)

Source: Bill Koski, Seeking Alpha

Kymriah approved first in R/R pediatric ALL; both Yescarta and Kymriah now FDA approved in 3L+ DLBCL; price is $475,000 per treatment for pediatric ALL and $373,000 for DLBCL

Leading CAR-T Products

	Kymriah (tisagenlecleucel) Novartis	Yescarta (axicabtagene ciloleucel) Gilead / Kite	JCAR017 Celgene / Juno
Indications (FDA approvals)	▪ R/R pediatric ALL (Aug 2017) ▪ 3L+ DLBCL (May 2018)	▪ 3L+ DLBCL (Oct 2017)	▪ Clinical development
Target / Format	▪ CD19/CD3ζ/4-1BB	▪ CD19/CD3ζ/CD28	▪ CD19/CD3ζ/4-1BB
Viral vector	▪ Lentivirus	▪ Gamma retrovirus	▪ Lentivirus
Cell population	▪ PBMC	▪ PBMC	▪ 1:1 CD4+ CD8+ T-cells
Inpatient / Outpatient	▪ JULIET: 25% of the patients were given their infusion outpatient (with monitoring)	▪ US Label: 7 days in the hospital post-infusion	▪ Outpatient potential
Price (per treatment)	▪ $475,000 for pediatric ALL ▪ $373,000 for DLBCL ▪ Includes leukapheresis	▪ $373,000 for DLBCL ▪ Does not include leukapheresis	▪ n/a

- Both Kymriah and Yescarta have ongoing trials in earlier lines of therapy; data for JCAR017 is encouraging
- Both Kymriah and JCAR017 utilize a 4-1BB domain, whereas Yescarta has a CD28 domain; all 3 target CD19

Source: groupH research and analysis, FDA product labels

Efficacy: CAR-Ts are generating considerable TAE excitement by demonstrating promising efficacy with response rates much higher than existing savage treatment options

Efficacy – R/R Pediatric B-ALL

Trial	Median No. Prior Treatments	Therapy	ITT / Corrected CR**
ELIANA	**3**	**Kymriah**	61/92 = **66%**
Von Stackelberg 2016	**2**	**Blinatumomab**	27/70 = **39%**
Locatelli 2017	**2**	**Blinatumomab**	25/40 = **63%**

"CAR-T therapy is transformative and represents a new method to treat cancer patients... It can bring a potentially life-saving option to patients whose care needs are currently unmet by existing therapeutics and who would otherwise receive high-cost, ineffective treatments"

– ASH Open Letter to CMS (June 25th, 2018)

Efficacy – 4L+ DLBCL

Trial	Median No. Prior Treatments	Therapy	Reported ORR	Reported CR*	ITT / Corrected CR**
ZUMA-1	**3**	**Yescarta**	**82%**	**54%**	52/111 = **47%**
JULIET	**3**	**Kymriah**	**53%**	**40%**	n/a
SCHOLAR-1 (historical control)	**3**	**Mix of salvage therapies**	**26%**	**7%**	**7%**

*CR rate represents an optimistic presentation of the results that violates the intention to treat principle because it is based on patients who received the infusion of CAR-T cells and does not include the patients who enrolled in the trials but did not receive the therapy because of manufacturing failures, death prior to infusion, or AEs

**Based on the number enrolled, not the number receiving the infusion with CAR-T cells

Source: ICER Final Evidence Report

Safety: life-threatening adverse events can emerge with current CAR-T treatments (e.g. cytokine release syndrome and neurotoxicities) that require ICU care if severe; this increases the cost of administering these therapies

Safety

Adverse Event	All Grades		Grades 3+	
	Kymriah [ELIANA]	Yescarta [ZUMA-1]	Kymriah [ELIANA]	Yescarta [ZUMA-1]
Cytokine Release Syndrome	79%	94%	49%	13%
Neurologic Toxicities	65%	87%	18%	31%
Fever	50%	86%	15%	16%
Encephalopathy	34%	57%	10%	29%
Headache	37%	45%	3%	1%
Hypotension	31%	57%	22%	15%
Hypoxia	24%	32%	18%	11%
Infections (unknown pathogens)	41%	26%	16%	16%
Viral infections	26%	16%	18%	4%
Bacterial infections	19%	13%	13%	9%
Fungal infections	13%	5%	7%	NR

The "adverse events are usually manageable but do increase the cost of this therapy as patients are typically required to be admitted as inpatients for treatment.

These inpatient stays must be factored into an appropriate reimbursement mechanism"

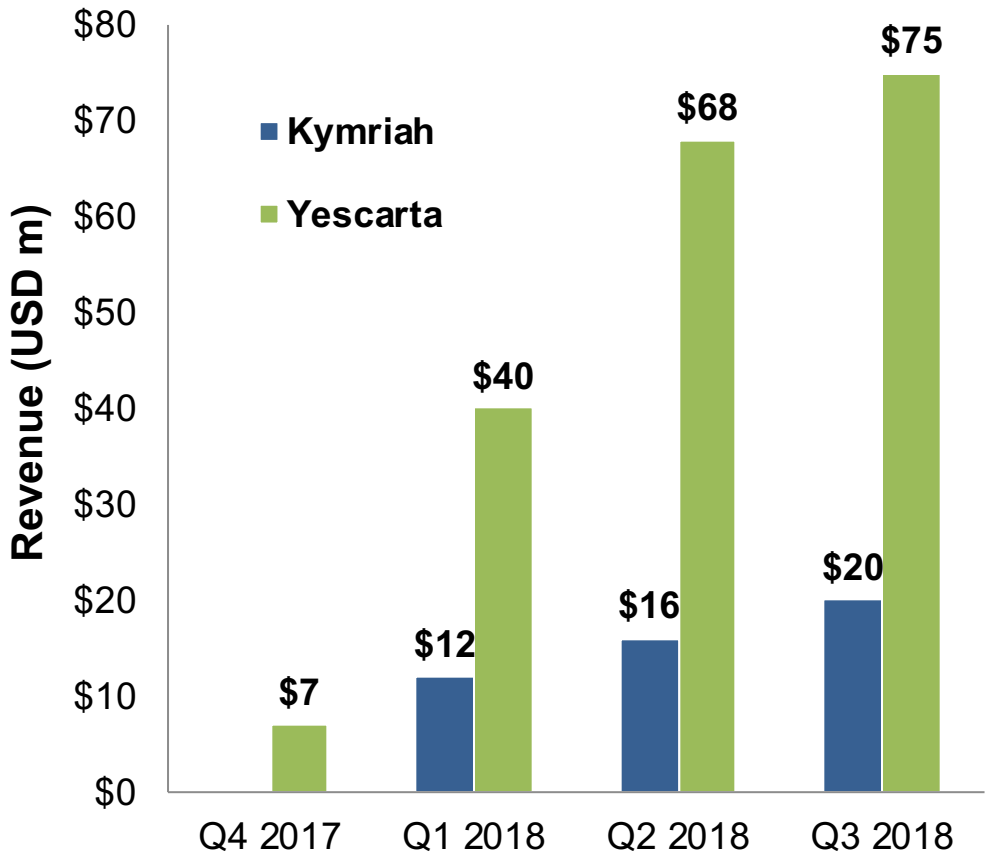
– ASH Open Letter to CMS (June 25th, 2018)

- Mitigation and management strategies for CAR-T Toxicity (CAR-TOX) are improving, leading to improved overall safety profile

Source: ICER Final Evidence Report

Despite considerable research, clinical and commercialization expenses, the combined Yescarta & Kymriah first year sales are less than $250m

Kymriah and Yescarta Revenue



Considerable Manufacturer Investment

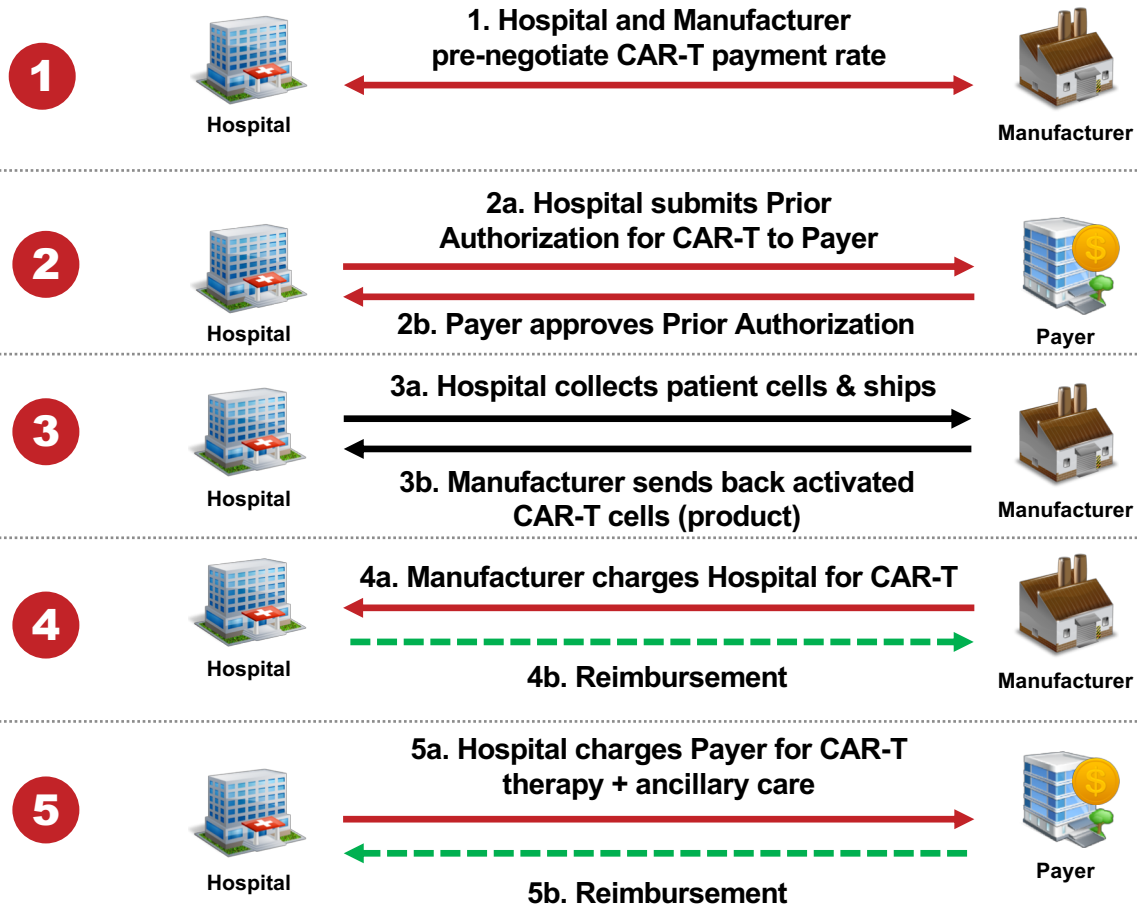
- Gilead's $11.9bn acquisition of Kite / Celgene's $9bn acquisition of Juno
- Technology development and clinical development costs
- Building manufacturing infrastructure – USA factories; plans to build an EU CAR-T manufacturing facility; expansion plans in the US

Source: groupH research and analysis, Seeking Alpha

Current Reimbursement Environment

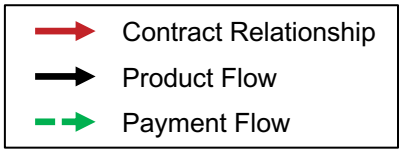
Under the current reimbursement framework, hospitals seek prior authorization from payers, ship patient's cells and receive activated CAR-T product, are billed by the manufacturer, and then seek reimbursement from payers

2018 CAR-T Reimbursement Process for Commercial Payers



Process difference for Government Payers

- Hospitals do not contact government payers to pre-negotiate reimbursement prior to initiating therapy
- Hospitals seek reimbursement after administering CAR-T from Medicare Administrative Contractors (MACs)
- Reimbursement amount will vary by site of care and how the claim is coded



Source: groupH research and analysis

Update: Jan 2019

Update: commercial payers provide CAR-T coverage, while Medicare provides coverage in the outpatient setting; until an NCA determination is made, Medicaid coverage differ by state

Jan 2019 CAR-T Reimbursement by Payer Type

Commercial Payers	Standard Medicare	Medicaid
▪ Reimbursement negotiations on case-by-case basis ▪ Prior authorization criteria: ○ Most payer PAs follow the product labels (e.g. two or more lines of systemic therapy) ○ Manufacturer-certified treatment centers ▪ **In-network hospital:** use current contracted rates for inpatient & outpatient services with drug paid separately (typically at cost or 6-10% above ASP) ▪ **Out-of-network hospital:** all treatment components (drug, collecting cells, post treatment care, etc) are pre-negotiated	▪ **Outpatient setting:** CMS coverage in outpatient setting (ASP + 6%) ▪ **Inpatient setting (2018):** no DRG for CAR-T, no approved NTAP, current outlier payment applicable ○ Current leukemia & lymphoma DRGs designed for chemotherapy ~$10k-35k	▪ Waiting for formal 2019 NCA decision ▪ Coverage decisions are currently state-by-state: ○ No formal document stating any CAR-T coverage: e.g. Arizona, Alaska ○ CAR-Ts on formulary, but no guidance published: e.g. Maine ○ Policy and reimbursement mechanism stated – separate CAR-T carve-out payment: e.g. NY, Mass, Indiana
✓ **Good coverage** **Few restrictions beyond product label** **Ad hoc mechanism – adequate for a small number of patients**	~ **Coverage differs significantly between inpatient and outpatient**	~ **Until NCA, coverage differs by state**

Source: groupH research and analysis

Total charges can rise considerably higher than the cost of CAR-T therapy, and costs can vary widely depending on the extent of adverse events such as CRS – average $1m per patient

Factors that Increase Total Therapy Charges

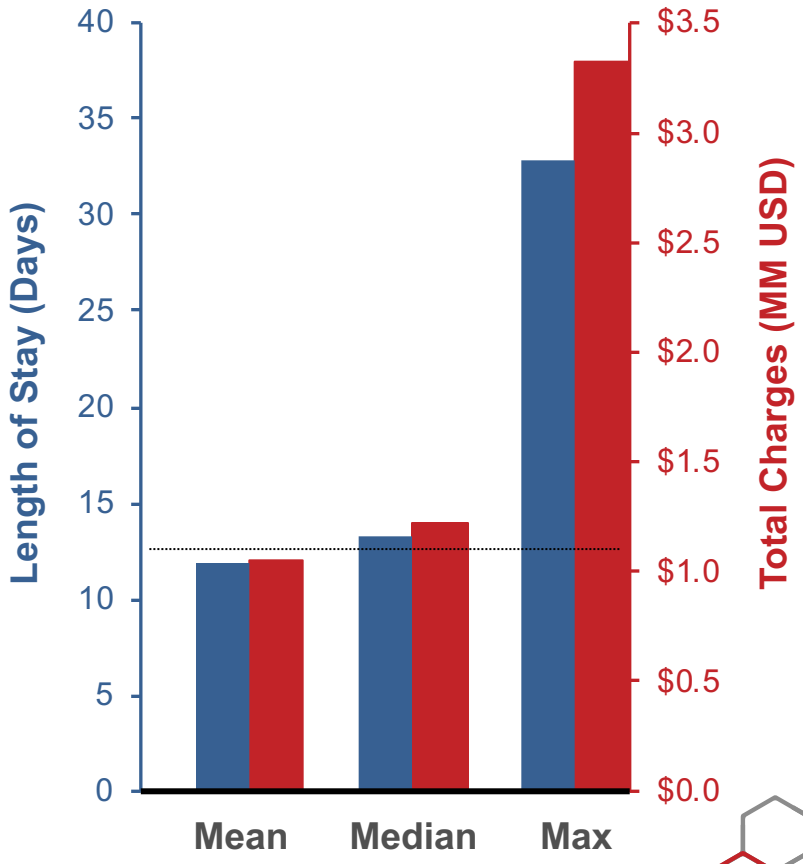
- **Toxicity management**: varies depending on severity of cytokine release syndrome, treating neurotoxicities, hospitalization (inc. ICU care), and other adverse events
- **Leukapheresis**: varies if patient's veins are compromised
- **Bridging treatments**: varies depending on disease progression

"Patients with with severe cytokine release syndrome may cost $50-100k for the hospital, and more billed to the payer"
– **Hospital P&T Pharmacist**

"There's the hospital stay, other ancillary lab costs, labor costs, and just managing just a very sick patient is very costly that could easily cost another $300k-400k"
– **Pharmacy Director, National Plan**

"It's hard for me to nail down a specific range, but certainly, we could see upwards of five figures for neurotoxicity stays"
– **Pharmacy Director, National Plan**

2018 CAR-T Therapy: Estimated Total Charges (n=21)



Source: groupH research and analysis, ASBMT + ASH Proposed CAR-T coverage and payment options (Nov 1st, 2018)

The low volume of CAR-T patients has enabled commercial payers to take a 'watch-and-wait' mentality until more data emerges

2018 CAR-T Commercial Payer Attitudes

Low payer volume of CAR-T cases

- Inefficient manual case-by-case approval process
- P&T review on merits of individual drug with no cross comparisons
- Lack of real world efficacy, safety, and cost by site of care data

Open access for both drugs & lack of preference in directing site of care

Source: groupH research and analysis

Hospitals carry significant financial burden by treating Medicare patients because only patients with commercial coverage have ultimately been profitable

Jan 2019 CAR-T Hospital Reimbursement Level

Patient's Plan Type	Impact on Hospital	Reimbursement Outcome for Hospital
Commercial	 *"We ended up getting reimbursed $720k. Which means we made around $300k on those patients. We were very surprised how much they were willing to pay"* **– Hospital P&T Pharmacist**	**Net Positive** – *Although payers are tightening reimbursement with more cases*
Medicare	 *"WIth Medicare, we're at least breaking even on the drug outpatient. We're probably losing money on any inpatient care. It's not sinking the ship at this point. If we started doing 100 of these, I think it would definitely be something that would be right in front of my eyes on my desk almost every morning"* **– Hospital VP of Finance**	**Mixed** – *break even (outpatient) to significant loss (inpatient)*
Medicaid	 *"Medicaid… I think there's only been one pediatric patient and we lost our shirt on it. I don't think Medicaid paid us more than $50k. We lost at least $400k"* **– Hospital VP**	**Mixed** – *coverage differs by state*

Source: groupH research and analysis

Hospitals with high-risk tolerance that wish to be at the 'cutting edge' of medicine are administering CAR-T, while remaining hospitals are forced to be more selective in which patients they treat

Hospital Risk Profiles

Low — Hospital Financial Risk Tolerance — High

Low Financial Tolerance

- Will only administer CAR-T to patients with verified & adequate reimbursement from payer
- Does not treatment standard Medicare or Medicaid patients due to reimbursement risk

Moderate Financial Tolerance

- Feels it should not turn away patients but does not have deep pockets for sustained loss
- Has treated Medicaid but significant losses likely means no further Medicaid patients until reimbursement improves

High Financial Tolerance

- Prestige of being 'cutting edge'
- Likely has 'deep pockets' from financial diversifications and rich donation base
- Treats all patients regardless of ability to pay because it's the "right thing"
- e.g. leading academic medical centers

Approach to selecting patients for treatment

"If a patient's finances aren't secure upfront, they're not getting treated"

"We're a community-based system that is trying to do the best we can without going bankrupt"

"We will provide the treatment to the patient, and take the risk on whether we can get reimbursed"

Source: groupH research and analysis

Risk-sharing: Novartis's risk-sharing approach for Kymriah in ALL is at an early stage – it is being slowly rolled out with providers and has been adopted by MassHealth Medicaid

Novartis risk-sharing approach for Kymriah in ALL: institutions will not be charged for the product if presence of leukemia is confirmed (>5% bone marrow blasts) within 28-35 days after infusion

Jan 2019 Status of Novartis CAR-T Risk-Sharing Model

Entity	Details	Status / Experience
Hospitals	▪ Some approved centers have been offered risk-sharing ▪ Hospitals need to opt-in to the agreement ▪ Rollout has been very recent, so signed hospitals have not yet used this agreement	Recently Rolled out
Medicare	▪ Officials cancelled the plan (July 2018) after it drew internal HHS scrutiny ▪ Scrutiny tied to Trump's attorney Michael Cohen's $1.2M healthcare consulting agreement with Novartis ▪ Administration lawyers expressed discomfort over how Novartis was influencing the arrangement (i.e. payment criteria)	In Discussion; Quietly Ended
Medicaid	▪ If drug does not work, Medicaid only pays for services associated with the treatment course, not the product ▪ First example: MassHealth ▪ Other example (not publically announced): New York (Yescarta only – remission assessment time frame unknown)	In Progress

Sources: groupH research and analysis, FiercePharma, Commonwealth Medicine

Summary: reimbursement reform is imperative if CAR-T therapy is going to live up to its exciting promise of providing a new standard of care in oncology

Commercial Patients | **Medicare Patients** | **Medicaid Patients**

CAR-T Hospital Implications

- Current no barriers – reimbursement levels and case-by-case approval is not impacting hospitals
- The "mixed" inpatient/outpatient reimbursement is limiting patients to a few hospitals willing to take financial risk
- Even "risk-taking hospitals" are reconsidering or limiting the number of Medicaid patients due to woeful reimbursement

Manufacturer Implications

- The high-touch reimbursement process is functioning at low patient volume, but if scale increases, management will be difficult, and could limit product uptake
- Reimbursement is a barrier holding back current CAR-T utilization potential for public payer patients
- If current reimbursement does not change, follow-on indications and next-generation products will also suffer commercially

Source: groupH research and analysis

Stakeholders' Needs & Assessment Framework

New reimbursement approaches for CAR-T therapies can be evaluated based on their ability to meet the needs of key stakeholders and ease of implementation

Assessment = Ability to Meet Stakeholders' Needs + Ease of Implementation

Enable patient access to new therapies without undue economic burden

Patients worry that out-of-pockets costs will be prohibitively high for new high-cost treatments.

Ensure providers are incentivized to administer therapies

Health care providers do not want to suffer burden with respect to working capital outlays at time of treatment, financial risk, or risk of outcomes for using new transformative therapies.

Ensure long-term value, given high cost

Payers are concerned about paying high up-front costs for therapies that do not yet have the evidence to support projected long-term benefits. Payers want patients to achieve the outcomes they are paying for.

Budget impact not a current concern

Budget impact is less of a concern in orphan indications, but becomes a more significant concern for therapies to treat larger populations.

Recognize the value of innovation/ therapeutic advances

Innovator companies invest substantial resources into the development, manufacture, launch and infrastructure of new therapies, are concerned that this investment may not be rewarded.

Be feasible to implement in a time frame to promote product adoption

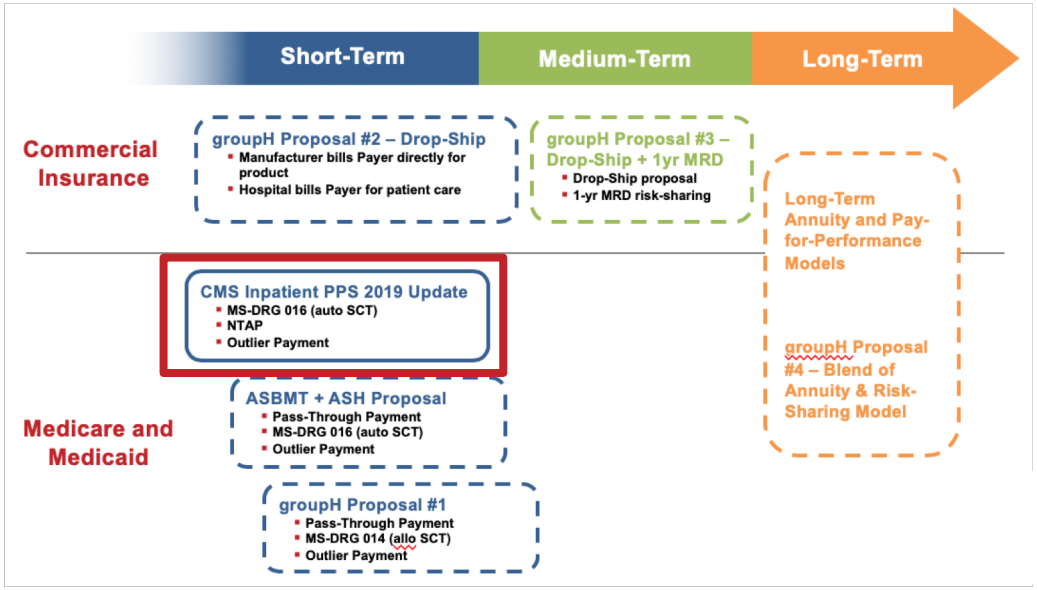
Solutions that could be implemented within current public and private payer systems are needed that do not impede patient access to innovative new therapies.

Changes in access, coding and payment policies and systems can take time.

A balance between short-term fixes and long-term solutions should be sought.

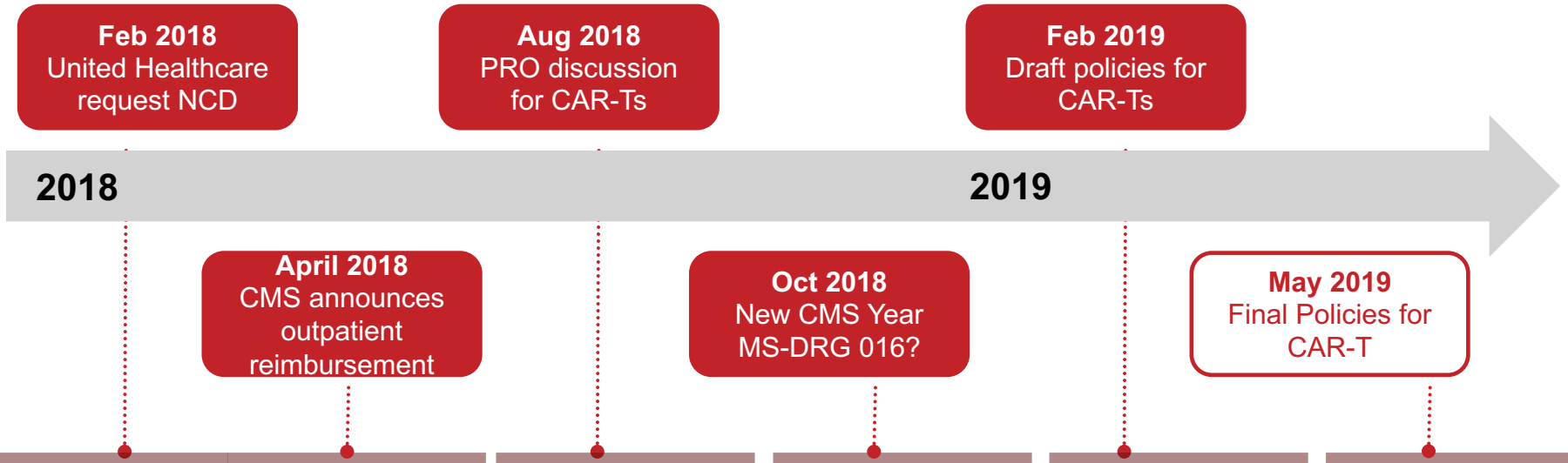
Source: groupH research and analysis, Alliance for Regenerative Medicine, Slocomb et al. 2017 IN VIVO

Short-Term Reimbursement: Medicare in 2019



Update: Feb 2019

CMS has been very active in CAR-T policy development, and outlined an interim proposal for 2019*; however, much uncertainty remains, with draft polices made Feb 2019 and finalization in May 2019



- United request NCD given their national footprint & wanting consistency for their MA business
- Manufacture believes NCD is not necessary
- Manufacturer fears MACs will not grant coverage while waiting for NCD decision
- NCD analysis signals restrictions for institutions

- On April 1st, Medicare capped Part B OOP to $1,340 + the deductible
- CMS announced the outpatient reimbursement for CAR-T at ASP +6% which is ~$400k for Yescarta & $500k for Kymriah in ALL

- Medicare Evidence Development & Coverage Advisory Committee (MedCAC) met Aug 22
- Committee mostly favorable of PROs at a high-level but manufacturer oppose PRO for decisions because they "aren't ready" yet

- October 1st is the start of the 2019 year for Medicare
- This is the official day that the proposed MS-DRG 016 can be used for CAR-T therapy + NTAP payment with a max of $186.5k
- No CCR of 1.0, pass through approved, or exempt PPS fix

- CMS released memo on Feb 15, 2019 stating Medicare coverage with a CED
- Coverage for both in/out patient CAR-T administration but providers need to track patients for up to two years
- CMS did not provide further guidance on reimbursement levels

- Finalization from the Feb 2019 draft expected by May 17th 2019 after a 30 day public comment period and 60 day evaluation time frame

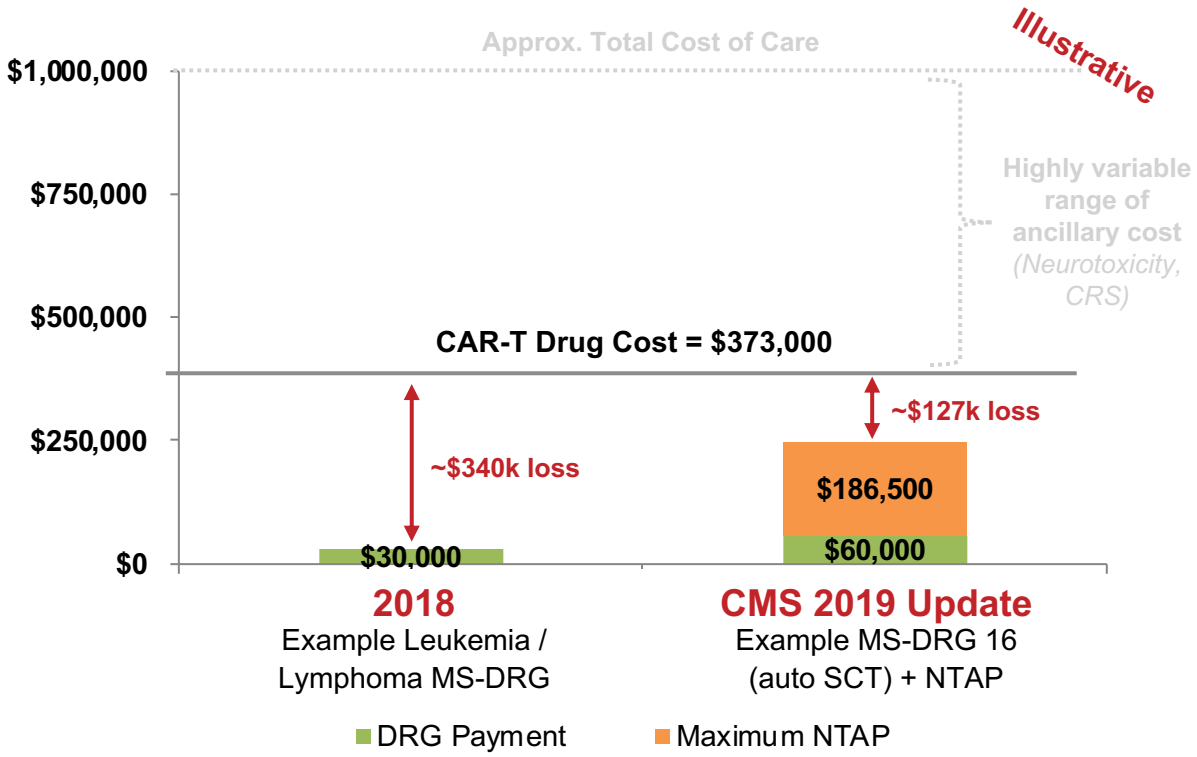
* Medicare 2019 year starts Oct 1st, 2018; Source: groupH research and analysis

The CMS update for 2019 allows an MS-DRG 16 payment, plus NTAP, and possible Outlier Payment for the inpatient setting; this reduces the loss made by providers, but still leaves them underpaid

CMS Inpatient PPS (IPPS) 2019 Update

- Payment of **MS-DRG 016** (auto SCT)
- May be augmented by the full **New Technology Add-on Payment** (NTAP)
- Providers could also receive an **Outlier Payment** (not illustrated since highly variable)

CMS Inpatient PPS Update for 2019



The CMS 2019 inpatient update is a significant improvement for providers, but still leaves hospitals with a ~$127k shortfall on the product acquisition cost

Source: groupH research and analysis; ASH Open Letter to CMS (June 25th, 2018); ASBMT + ASH Proposed CAR-T coverage and payment options (Nov 1st, 2018)

Hospitals need to mark-up CAR-T price significantly in order to achieve the max NTAP payment, but many hospitals may not know to do this and/or wish to be seen marking up so significantly

Illustrative Example of 2 Hospitals – 110% vs. 400% CAR-T Mark-Up

	Hospital A 110% CAR-T Mark-Up	**Hospital B** 400% CAR-T Mark-Up
Assumptions	**Wage Index**: 1.0, **Hospital CCR:** 0.25, **CAR-T Drug Cost:** $373,000 **MS DRG 016 Base Payment** *w/ no Hospital adjustment:* $39,951, **Fixed Loss Outlier Amount:** $25,769	

Hospital Charges	▪ **CAR-T Cost w/ Mark-Up:** $413,300
	▪ **Non-Drug Inpatient Charges:** $228,000
	▪ **Total Charges:** $638,300
	▪ **Hospital Cost (Charges x CCR):** $159,575
	  ▪ **Non-Drug Cost:** $57,000
		▪ **CAR-T Cost w/ Mark-Up:** $1,492,000
		▪ **Non-Drug Inpatient Charges:** $228,000
		▪ **Total Charges:** $1,720,000
		▪ **Hospital Cost (Charges x CCR):** $430,000
		  ▪ **Non-Drug Cost:** $57,000

NTAP Payment	▪ **Hospital Cost:** $159,575 ▪ **Excess Cost** (Hosp. Cost – DRG): $119,624 ▪ **50% of Excess Cost:** $59,812 ▪ **NTAP CAP (50% of CAR-T):** $186,500 ▪ **Estimated NTAP** (Lower of NTAP vs 50% Excess cost): **$59,812**	▪ **Hospital Cost:** $430,000 ▪ **Excess Cost** (Hosp. Cost – DRG): $390,049 ▪ **50% of Excess Cost:** $195,025 ▪ **NTAP CAP (50% of CAR-T):** $186,500 ▪ **Estimated NTAP** (Lower of NTAP vs 50% Excess cost): **$186,500**
Outlier Payment	▪ **Hospital Cost:** $159,575 ▪ **Outlier Threshold** (MS-DRG PMT + NTAP + Fixed Loss Amount): $125,532 ▪ **Outlier Payment Step 1** (Hospital Cost – Outlier Threshold): $34,043 ▪ **Final Outlier Payment** (80% of Step 1): **$27,234**	▪ **Hospital Cost:** $430,000 ▪ **Outlier Threshold** (MS-DRG PMT + NTAP + Fixed Loss Amount): $252,220 ▪ **Outlier Payment Step 1** (Hospital Cost – Outlier Threshold): $177,780 ▪ **Final Outlier Payment** (80% of Step 1): **$142,224**
Total Payments	**$126,997** (MS-DRG 016 + NTAP + Outlier Payment)	**$368,675** (MS-DRG 016 + NTAP + Outlier Payment)
Profit /Loss	**$303,003 Loss** (Drug Cost + Non-Drug Cost – Total Reimbursement)	**$61,325 Loss** (Drug Cost + Non-Drug Cost – Total Reimbursement)

Source: groupH research and analysis, ASBMT

New Slide: Feb 2019

February 15th 2019: CMS Memo states that Medicare will provide CAR-T coverage with evidence development (CED) – providers must participate in tracking outcomes over 2 years

Details of CMS Memo

- **CMS provided coverage details and requirements for Medicare coverage, but gave no updates to reimbursement mechanisms or amounts**
- **CMS will cover CAR-T in both the in and outpatient setting**
- **In order for to receive reimbursement, institutions must use CMS specified measurement tools / PROs & record results in approved registries**
  - Patients will be assessed at baseline and post treatment: 3 months, 6 months, 12 months and 24 months
  - No guidance on implementation timing
- **CMS will use the data to determine the long-term coverage policy comparing to clinical trial results and current SoC to determine optimal patient beneficiaries**

Implications

- **Providers will still experience financial loss on CAR-Ts product costs when used in the inpatient setting**
- **The reporting requirements could prove to be too burdensome for some institutions**
- **The CED requirement gives providers a legal route to opt-out of providing CAR-Ts to Medicare patients**

"Patients in rural areas have difficulty accessing authorized CAR T-cell therapy centers; with this CED requirement, I think there will be places that will choose not to do it (provide CAR-T for Medicare patients)"
– Joseph Alvarnas, MD – Government Affairs & employer Strategy (City of Hope)

- **Previous CEDs have been difficult to implement and failed to generate the evidence CMS needed to make coverage determinations**

Source: groupH research and analysis

The CMS 2019 inpatient update is a significant improvement for providers, but still leaves hospitals with a shortfall on the product acquisition cost

Assessment of CMS Inpatient PPS Update for 2019

Patients
Ensure patient access; minimize economic burden

Hospitals
Ensure not disincentivized to provide Rx

Payers*
Balances price vs. risk vs. long-term outcomes

Manufacturers
Recognizes value of innovative therapeutics

Implementation
Ease of implementation

2019 CMS
MS-DRG 016 (auto SCT)
+NTAP
+Outlier Payment

No change to existing patient cost-share structure

Significant loss on Medicare inpatient remains

Concerns over long-term outcomes not addressed

Manufacturers receives full price, but some risk remains for hospitals therefore limiting uptake

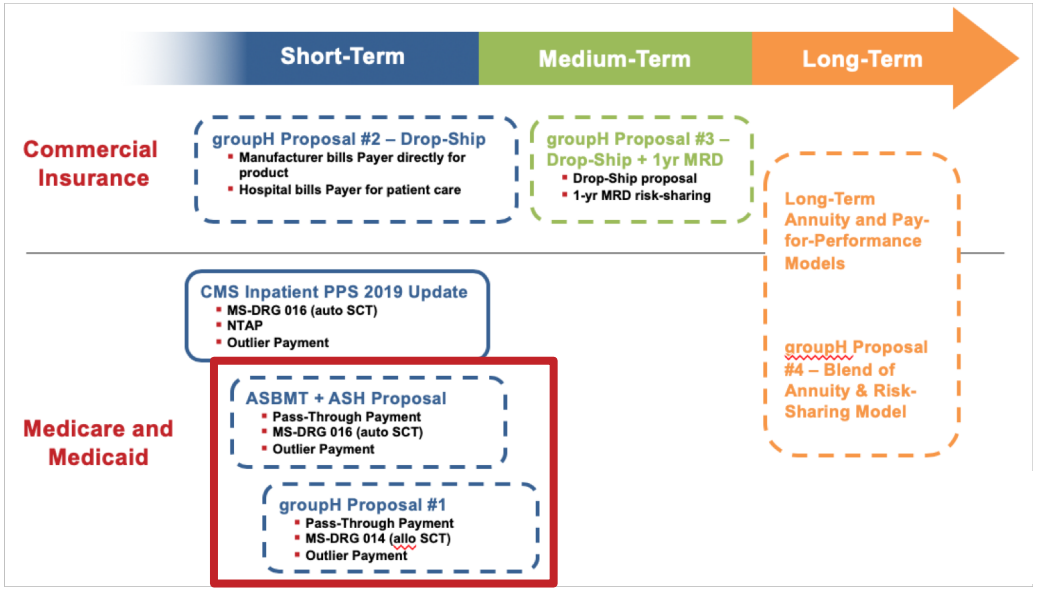
CMS plans already announced

Although better than using Leukemia DRGs, over $100k loss on product is significant

*We assume that Medicare payers have the same stakeholder needs as commercial payers
Source: groupH research and analysis

Less Favorable ◯ ⟷ ● More Favorable

Short-Term Reimbursement Proposals: Medicare in 2019

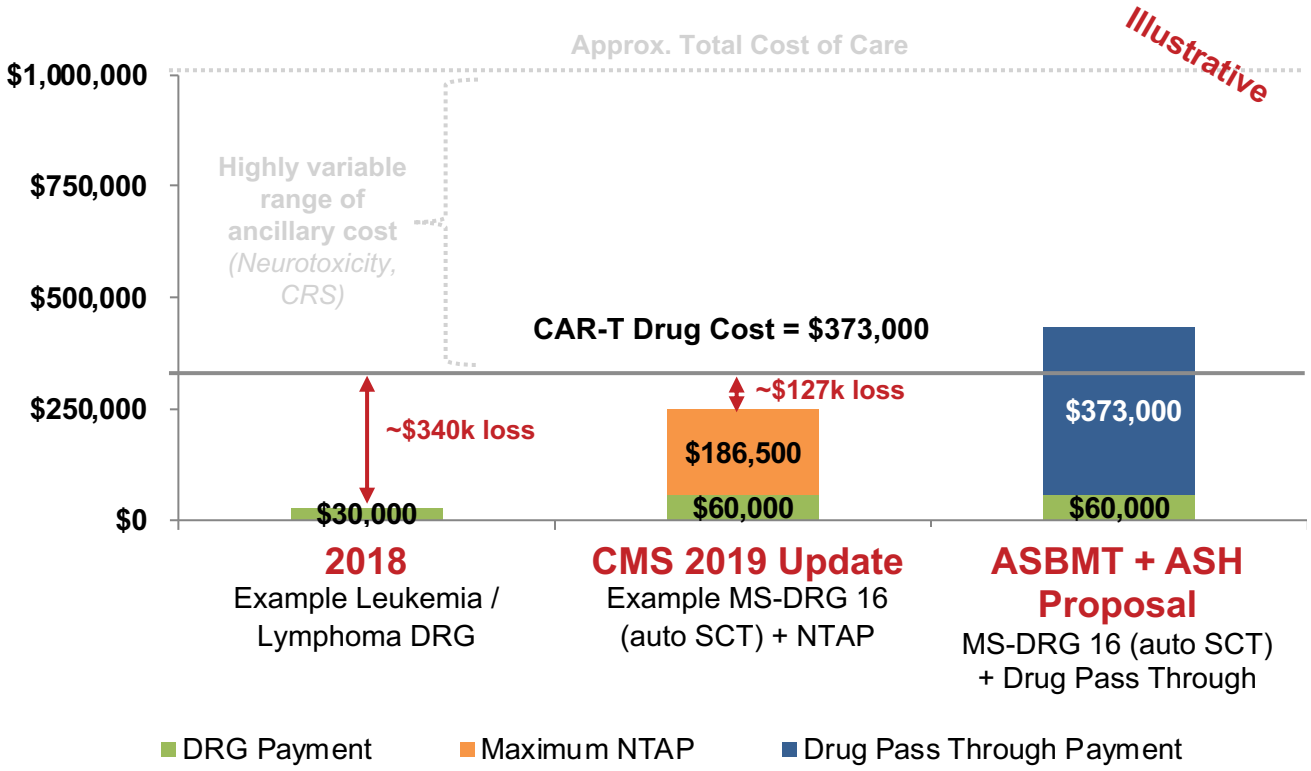


ASBMT + ASH proposal: reimbursement through a Drug Pass Through Payment, rather than a NTAP (in addition to CMS MS-DRG 16); this allows for drug cost recovery, but still leaves a shortfall on the cost of care

ASBMT + ASH Proposal

- Establish a **Pass-Through Payment** for the cost of CAR-T cells
- Use **MS-DRG 016** (auto SCT) with its current **Outlier Policy** to cover some of the cost of care

ASBMT + ASH Proposal (June, 2018)



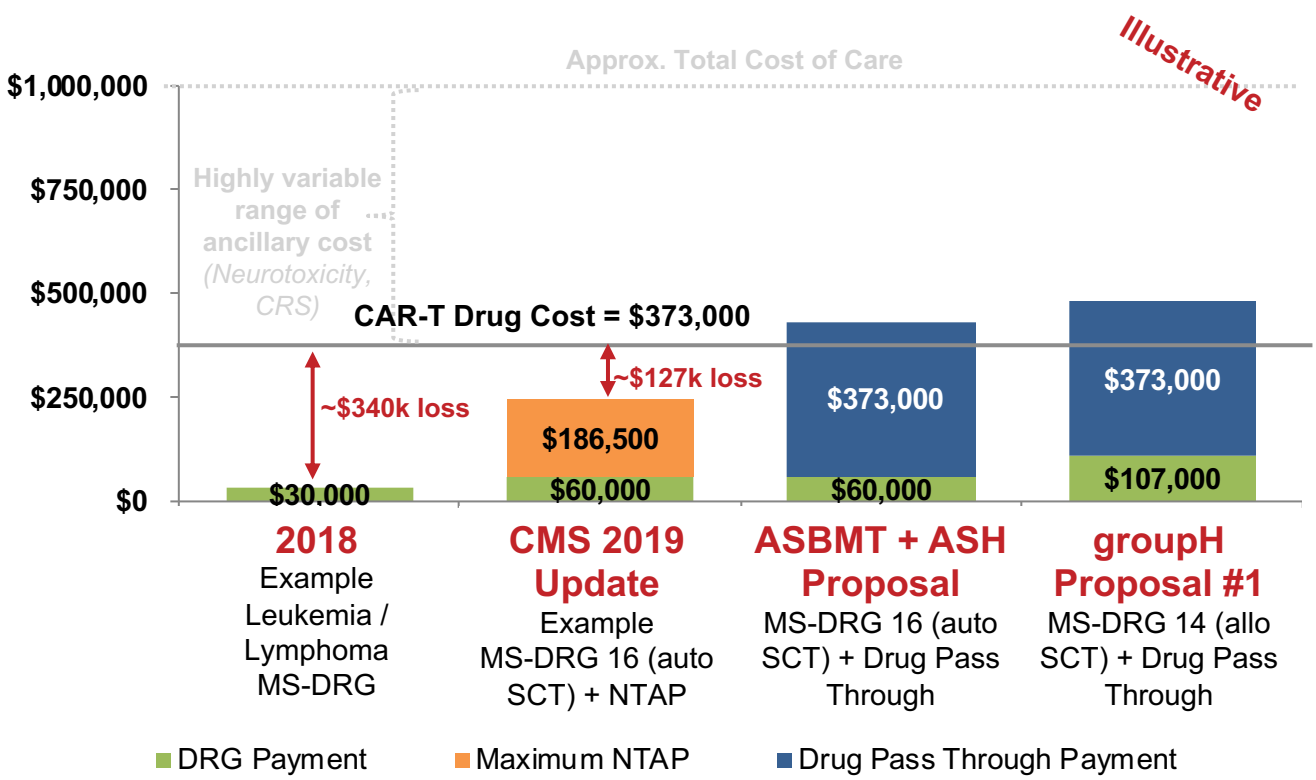
This proposal allows for total drug cost recovery, but still leaves a shortfall on the cost of care (since fewer autoSCT patients experience adverse events that require admission to the ICU, than CAR-Ts)

Source: groupH research and analysis; ASH Open Letter to CMS (June 25th, 2018); ASBMT + ASH Proposed CAR-T coverage and payment options (Nov 1st, 2018)

groupH Proposal #1: reimbursement through a Drug Pass Through Payment, but use DRG 14 (allo SCT) rather than DRG 16 (auto SCT); this allows for total drug cost recovery + further minimizes hospital losses

groupH Proposal #1

- Establish a **Pass-Through Payment** for the cost of CAR-T cells
- Use **MS-DRG 014** (allo SCT) with its current **Outlier Policy** to cover some of the cost of care



This proposal increases the payment to cover the cost of care, since MS-DRG 014 reflects the increased costs of treating and managing complications of allo SCT

Source: groupH research and analysis; ASH Open Letter to CMS (June 25th, 2018); ASBMT + ASH Proposed CAR-T coverage and payment options (Nov 1st, 2018)

New Slide: Feb 2019

MS-DRG 16 (auto) is a better match to CAR-Ts since treatment is autologous, but provides a lower level of reimbursement; MS-DRG 14 (allo) provides greater reimbursement levels and is a better match to length of stay and intensity of complications

	MS-DRG 16 (Autologous SCT)	**MS-DRG 14** (Allogenic SCT)
PROs	▪ Procedurally closer to current CAR-T process ▪ CMS believes that an underpayment is a message to industry *(2nd Gen CAR-Ts and Gene Therapies)* that they will not accommodate and encourage industry's high list prices	▪ Length of stay and intensity of complications from allogenic stem cell transplantation such as GvHD is more similar to CAR-T ▪ Higher reimbursement that could result in a net profit to institutions with a drug carve out payment would facilitate faster data collection to determine coverage and reimbursement levels
CONs	▪ Autologous SCT has lower intensity complications as well as fewer complications compared to CAR-T resulting in a DRG payment that would be inadequate for CAR-T care costs ▪ Inadequate reimbursement would likely result in less Medicare CAR-T cases slowing the data collection process for coverage and determining reimbursement levels to create a CAR-T DRG	▪ MS-DRG 16 is a closer procedure equivalent ▪ Fear that if CAR-T became more common and hospitals became more comfortable they would use procedure on less sick patients, thus potentially lower HSCT reimbursement rate that ASBMT fought for many years to increase the reimbursement rate

Source: groupH research and analysis

Hospital feedback is most positive for groupH Proposal #1 – it minimizes their losses, and might even create a minor profit in some circumstances

Feedback on 2019 Medicare Proposals

Proposal		
2019 CMS MS-DRG 016 (auto SCT) +NTAP +Outlier Payment		*" I don't know how hospitals will be able to provide care with that significant amount of loss"* **– Hospital P&T Pharmacist**
ASMBT + ASH MS-DRG 16 (auto SCT) +DPTP		*"I do think the DRG payments don't allow for the full recovery of the actual cost. At least this allows a little bit of a better model where the cost of the drug is not being lost"* **– Hospital P&T Pharmacist**
groupH #1 MS-DRG 14 (allo SCT) +DPTP		*"I think it's better of the other two alternatives. Relatively speaking allogenic transplant is about double an auto transplant cost. CRS tends to be about anywhere from 1-3 weeks while allogeneic transplant usually is 2-3 week inpatient admission"* **– Hospital P&T Pharmacist**

Unlikely that low financial risk tolerance hospitals will treat Medicare patients inpatient

Moderate financial risk tolerance hospitals appreciate the loss limit as they wait for a longer term reimbursement mechanisms

Could potentially be a minor profit for hospitals

Source: groupH research and analysis

Both proposals are relatively easy to implement and aim to address hospital reimbursement shortfalls; however, none address payers' long-term value needs

Assessment of 2019 Medicare Proposals





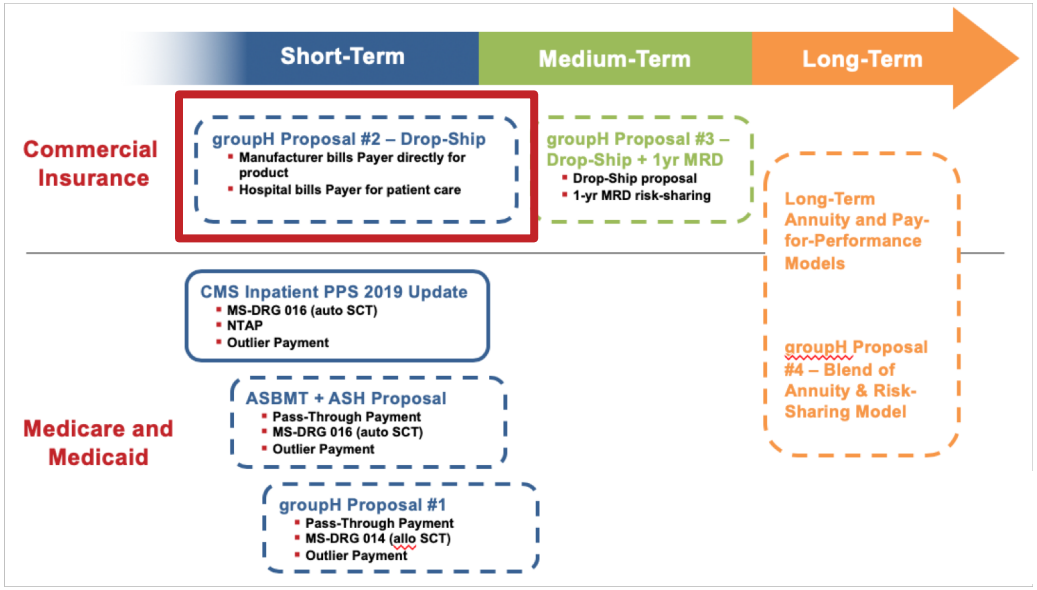
Proposal	**Patients** Ensure patient access; minimize economic burden	**Hospitals** Ensure not disincentivized to provide Rx	**Payers*** Balances price vs. risk vs. long-term outcomes	**Manufacturers** Recognizes value of innovative therapeutics	**Implementation** Ease of implementation	
2019 CMS MS-DRG 016 (auto SCT) +NTAP +Outlier Payment	*No change to existing patient cost-share structure*	*Significant loss on Medicare inpatient remains*	*Concerns over long-term outcomes not addressed*	*Manufacturers receives full price, but some risk remains for hospitals therefore limiting uptake*	*CMS plans already announced*	**Although better than using Leukemia DRGs, over $100k loss on product is significant**
ASMBT + ASH MS-DRG 16 (auto SCT) +DPTP	*No change to existing patient cost-share structure*	*Product cost recovered, but small loss remains if MS-DRG 16 not sufficient to cover ancillary costs*	*Concerns over long-term outcomes not addressed*	*Manufacturers receives full price; access hurdles lessened*	*Would require CMS policy to be updated*	**Improvement from 2019 CMS update but not as good as the groupH**
groupH #1 MS-DRG 14 (allo SCT) +DPTP	*No change to existing patient cost-share structure*	*Product cost recovered. MS-DRG 14 could be sufficient to cover ancillary costs for standard cases*	*Concerns over long-term outcomes not addressed*	*Manufacturers receives full price; access hurdles further reduced*	*Would require CMS policy to be updated*	**The best of the 3 proposals Could potentially be a minor profit for hospitals**

*We assume that Medicare payers have the same stakeholder needs as commercial payers

Source: groupH research and analysis

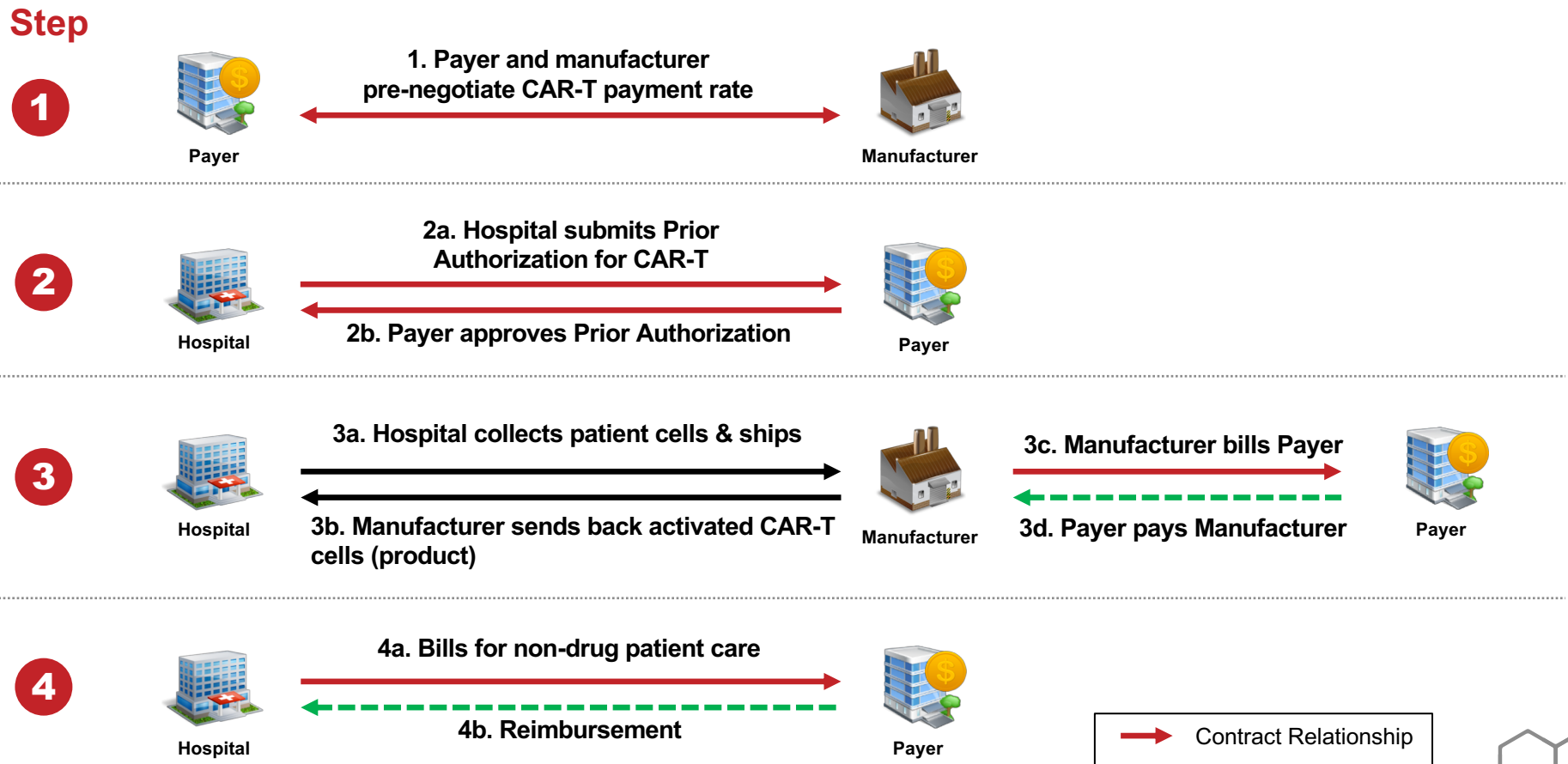
Less Favorable ⟷ More Favorable

Short-Term Reimbursement Proposals: Commercial Payers



groupH proposal #2: under the Drop-Ship Model, hospitals are not required to purchase the therapy – payers reimburse manufacturers directly

The Drop-Ship Model for Commercial Payers



Source: groupH research and analysis

New Slide: Feb 2019

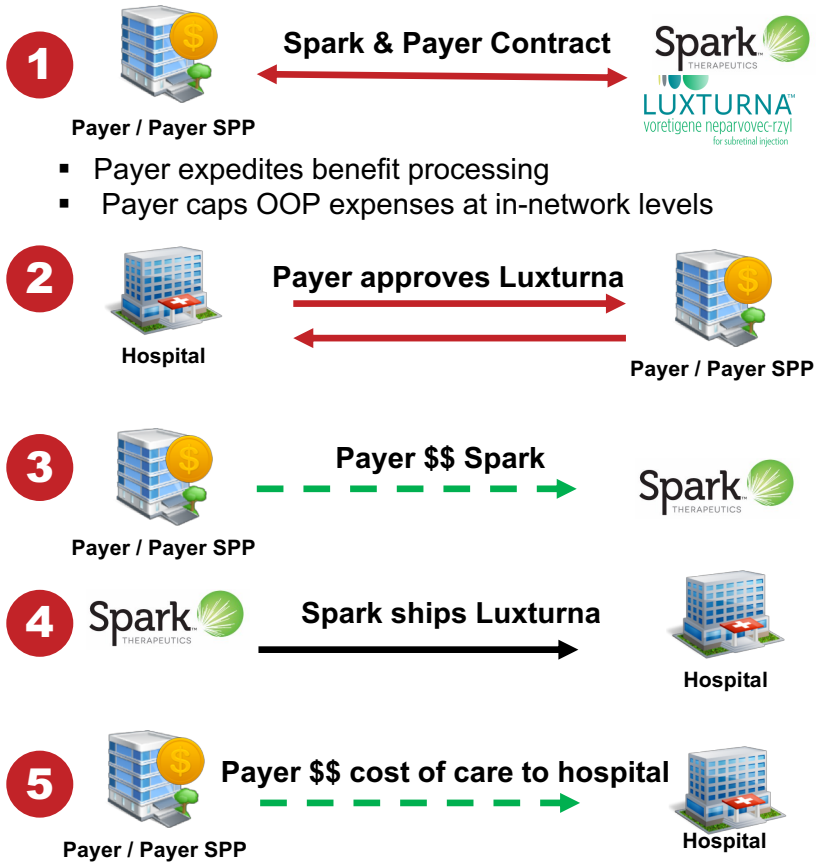
Spark Therapeutics Luxturna employs a similar distribution model to Drop-Ship where providers are not at financial risk for product procurement

The Biogen Spinraza experience may have influenced Luxturna's distribution model

"Many health centers did not want to buy Spinraza because they didn't want to stock it. It has special handling requirements, and if it's stored improperly or a vial is broken, that center is out "hundreds of thousands of dollars" **Steve Miller, Chief Medical Officer at Express Scripts**

"We want to be flexible for however payers and providers want Spinraza distributed. We dispense it from Accredo Specialty Pharmacy in a patient-specific dose that's shipped directly to the procedure room for administration by a neurologist or we also sell Spinraza through our distribution company, CuraScript Specialty Distribution. We'll take the holding risk" **Steve Miller, Chief Medical Officer at Express Scripts**

Luxturna Model bypasses traditional "Buy & Bill"



Source: groupH research and analysis

Both payers and hospital executives view the Drop-Ship Model favorably

Feedback on Short-Term Commercial Payer Proposal

Commercial Payers

One payer highlights that they can negotiate directly with the manufacturer

"The product needs to be carved out from the contract and not put the hospital at risk. The plan will negotiate a discount directly with the manufacturer"
– **Medical Director, National Plan**

Another payer was positive and sees no issues with Drop-Ship – they use the model for other drugs

"I can't see why drop-ship wouldn't work, the model already in place with many other therapies. It's just not the way CAR-T manufacturers launched their products"
– **Pharmacy Director, National Plan**

Oncology Hospitals

Keen to eliminate the product acquisition risk and just be paid for the administration

"It takes us out of the middle of negotiating between the insurance company and the manufacturer. If we can get out of being the drug middle man, I'll be real happy"
– **Hospital VP Finance**

"If you removed the risk of getting reimbursement for the cells via drop-ship with the financial deal outside of the environment of the hospital so all the hospital has to do is receive said cells and treat the patient with them, I think there's a huge opportunity there"
– **PPS Exempt VP**

Source: groupH research and analysis

The Drop-Ship Model reduces the impact on hospitals' working capital and enables payers to negotiate with manufactures for a better price; it does not address payers' concerns regarding outcomes

Assessment of Short-Term Commercial Payer Proposal

Patients
Ensure patient access; minimize economic burden

Hospitals
Ensure not disincentivized to provide Rx

Payers
Balances price vs. risk vs. long-term outcomes

Manufacturers
Recognizes value of innovative therapeutics

Implementation
Ease of implementation

Proposal	Patients	Hospitals	Payers	Manufacturers	Implementation
2019 CMS					
groupH proposal #2: Drop-Ship Model	 *No change to existing patients cost-share structure (patients likely hit OOP max prior to CAR-T therapy)*	 *Does not pay the CAR-T acquisition cost, which frees working capital* *Bigger impact for hospitals with lower capital reserves* *However, hospitals not able to make a profit on CAR-T product*	 *Gives payers stronger buying power and ability to negotiate price by negotiating directly with manufacturers* *Does not solve for payer concerns regarding long term outcomes*	 *Although price may be discounted, increase in volume from hospital utilization due to elimination of CAR-T cell reimbursement provides significant net financial boost*	 *Quick / easy to implement* *Similar to established model used with implantable cardioverter defibrillators (ICD) & emerging high cost gene therapies (Luxturna & Spiraza)*

Easy to implement

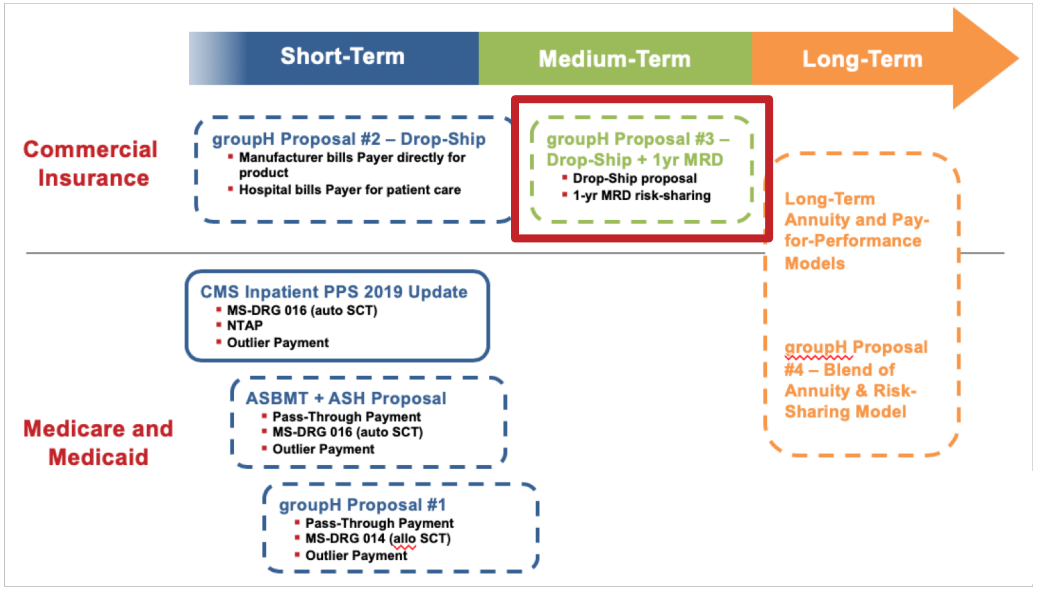
Reduces the impact on hospitals' working capital

Payers can negotiate with manufactures for better price

Less Favorable ○ ⟷ ● More Favorable

Source: groupH research and analysis

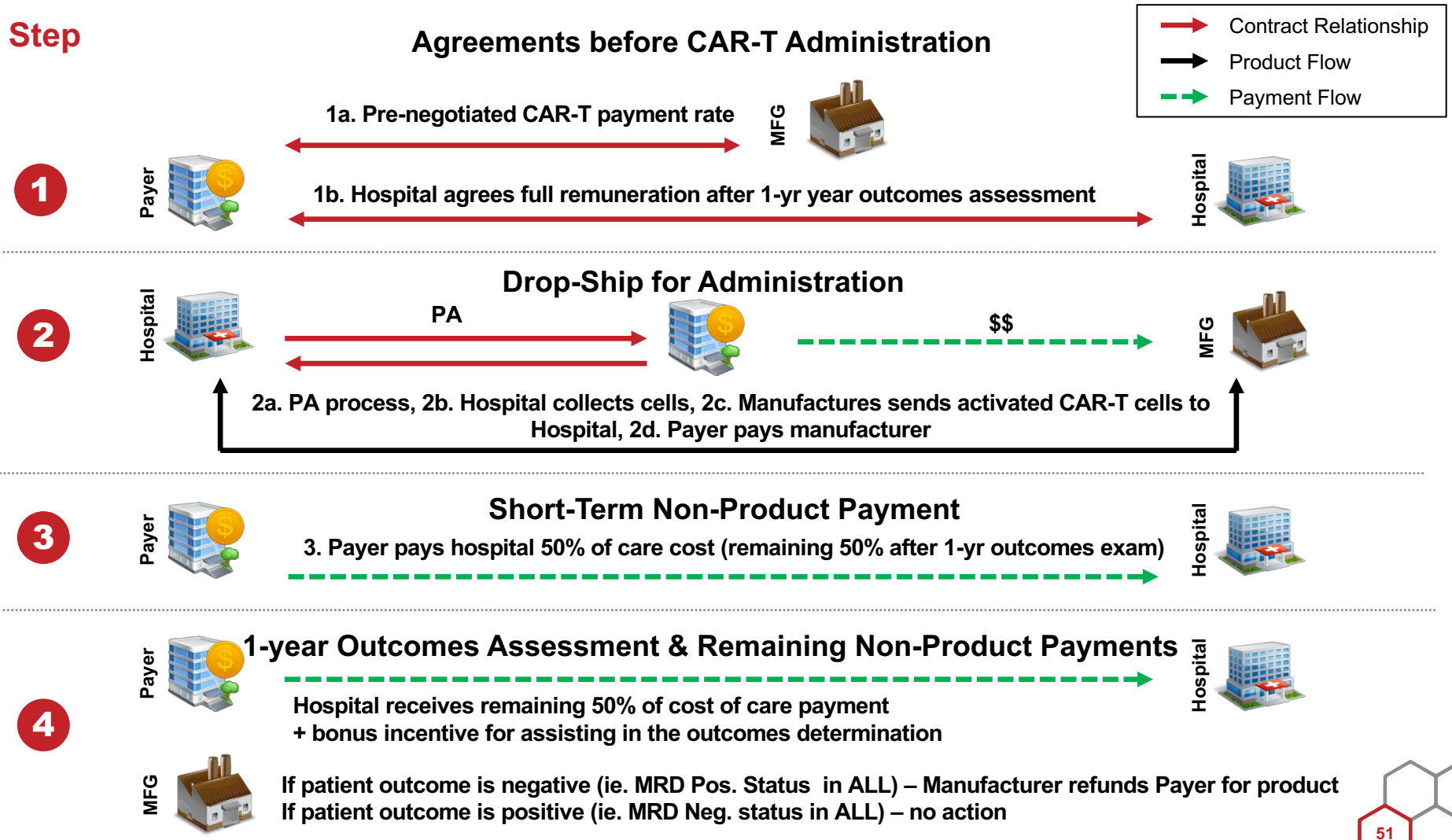
Mid-Term Reimbursement Proposals



Update: Feb 2019

groupH proposal #3 builds on the Drop-Ship model and incorporates risk-sharing through a 1-yr outcomes assessment

The groupH Mid-Term Payment Model



Source: groupH research and analysis

groupH proposal #3 (Mid-Term Payment Model) is easy to implement after Drop-Ship is established and accommodates both hospitals' and payers' needs

Assessment of Mid-Term Payment Model

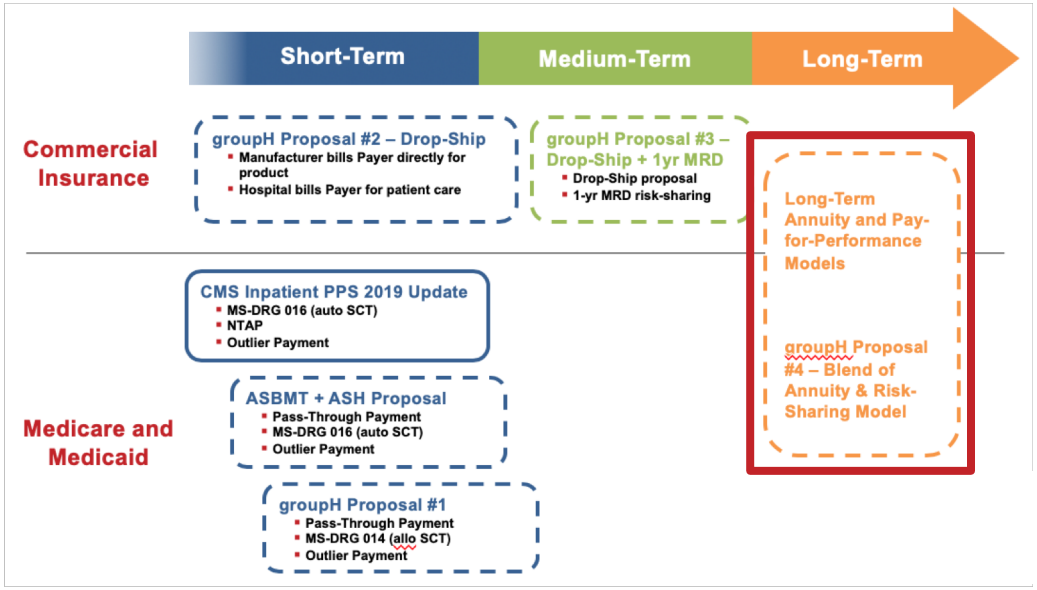
Proposal	Patients Ensure patient access; minimize economic burden	Hospitals Ensure not disincentivized to provide Rx	Payers Balances price vs. risk vs. long-term outcomes	Manufacturers Recognizes value of innovative therapeutics	Implementation Ease of implementation
Drop-Ship Model					
groupH proposal #3: Drop-Ship +1-yr Outcomes Assessment	*No change existing to patients cost-share structure*	*Does not pay the CAR-T acquisition cost, which frees working capital* *Bonus payment should offset extra hassle of delayed payment*	*Payers negotiate price directly with manufacturers* *Addresses payer concerns regarding longer outcomes and value*	*Outcomes agreements may help ease access & result in product placement driving volume* *Potential for financial risk since manufacturers will be not receive compensation for poor outcomes*	*Quick / easy to implement after drop ship is established* *Timeframe short enough to fit within Payer & hospital accounting systems*

Achievable model that improves Drop-Ship to address payer long-term value concerns

Less Favorable ⟷ More Favorable

Source: groupH research and analysis

Long-Term Reimbursement Proposals



Annuity and Risk Sharing / Pay-for-Performance Models are commonly proposed to spread the cost of therapies that provide a durable response from a single administration (such as gene and cell therapies)

Annuity

Description

- Installment payments spread over a pre-determined time period (e.g. monthly, annual for certain pre-specified number of periods or remaining life of patient)
- Payments may be based on or independent of amount of therapy dispensed on initial administration (Wilson & Brennan 2014)
- Payment terms would need to be developed that allow payers to spread out, under generally accepted accounting principles, high upfront costs of curative therapy over more of the years in which the benefits (and cost savings) of such interventions will be realized by both patients and payers alike (Gottleib 2014)

Pay-for-Performance

Description

- Payment amount adjusted depending on whether a pre-specified health outcome is achieved
- Net pricing mechanism can include discounts on future payments or rebates by innovator to payers
- This model shares risk between the manufacturer and the payer and rewards manufacturers for maintaining patients' health over a period of time

Examples

- Strimvelis launch in Italy includes one-time payment with limited risk-sharing provision common to specialty drugs
- A pay for performance arrangement is currently in place for ChondroCelect from TiGenix, a tissue engineered product for the repair of knee cartilage. The manufacturer provides a full refund if the product fails in Year 1, 75% in Year 2 and 50% after three years. (Carr & Bradshaw 2016)

Source: Adapted from Alliance for Regenerative Medicine, Slocomb et al. 2017 IN VIVO

Annuity Model: despite the many benefits, structural changes are needed in the US system before they can be implemented (e.g. Medicare and Medicaid rules)

PROs

- Potential to reward innovation and to better align costs with the time period over which benefits are delivered to the patient
- Payers – reducing up-front budget impact to the payer
- Patients – reduce initial cost as a barrier

CONs

- Seller must reach agreement on payment amount and duration with the purchaser
- Payer accounting rules will likely need to change to comply with these payment arrangements
- Harder to implement for patients with commercial insurance, since they tend to switch plans (or become Medicare eligible) → could mean that a patient is covered by one insurer with the costs of treatment continuing to be paid for by a prior payer
  - Easier to implement with Medicare and Medicaid – whose enrollees stay with the plan over longer periods of time
- Potential impacts on statutorily mandated discounts
- Does not address payer's long-term outcomes concerns

Source: Adapted from Alliance for Regenerative Medicine, Slocomb et al. 2017 IN VIVO

Pay-for-Performance: structural changes are also needed to implement these risk-sharing deals, in additional to outcomes data on which to model the deal

PROs

- Addresses payer concerns regarding long-term outcomes and value
- These arrangements may be attractive for innovators in cases where evidence/ predictors of durable effect are apparent in the short-term (several months to a couple of years) and may have already been characterized in clinical trials
- Many products are likely to have data registries that patients will be strongly encouraged to participate in for post-treatment follow-up, beyond post-marketing regulatory requirements, providing a means of data collection on product performance in aggregate and for individual patients that, with appropriate permissions and data safeguards, could be shared with all public and private payers in performance-based arrangements

CONs

- Manufacturer and payer must agree on the definitions of product performance, product value under uncertainty, and payment amount and schedule / duration
- Payer accounting rules will likely need to change to comply with these payment arrangements
- Harder to implement for patients with commercial insurance, since they tend to switch plans (or become Medicare eligible) → could mean that a patient is covered by one insurer with the costs of treatment continuing to be paid for by a prior payer
  - Easier to implement with Medicare and Medicaid – whose enrollees stay with the plan over longer periods of time
- Potential impacts on statutory state discount programs (Medicaid Best Price)
- Needs to implement patient & provider incentives for obtain longitudinal data for outcomes tracking
- Lack of long-term outcomes data for CAR-Ts

Source: Adapted from Alliance for Regenerative Medicine, Slocomb et al. 2017 IN VIVO

Adopting annuity and performance-based risk-sharing models will take several years to implement

Barriers to Alternative Reimbursement Models and Proposed Solutions

Barrier	Barrier Description	Solutions
Medicaid Best Price	▪ Manufacturers must report pricing data to the federal government, and Medicaid be given the 'best price' possible ▪ This rule may inhibit manufacturers tying price to outcomes	(1) CMS has the authority to address this issue through demonstration waivers (2) Federal legislation may be necessary to codify certain payments as exempt from 'best price'
Anti-Kickback Statute (AKS)	▪ AKS prohibits any remuneration for the referral of items or services by federal health care programs ▪ Outcomes-based payments have the potential to fall afoul of the AKS	(1) Office of the Inspector General (OIG) enforces compliance (2) OIG guidance and coordination with CMS (3) Establish new 'safe harbors' to enable alternative payment mechanisms
Payment Over Time	▪ Government payers (Medicare and Medicaid) generally require payment at the time of treatment ▪ Under generally accepted accounting rules for financial reporting, an annuity payment model could require insurers to recognize the entire cost of the treatment at the time the therapy was administered, even though full payment has not yet been made	(1) Pursue guidance from CMS to ensure proposed models allow for cost over time (2) Explore innovate models via Center for Medicare and Medicaid Innovation (3) Federal legislation to eliminate state-to-state variability
Portability	▪ Patients may move from one insurance provider to another; at present, if an insurer enters into a annuity or performance based arrangement intended to span several years, the insurer could be forced to continue payments for an individual who is no longer a member	(1) Create arrangements that allow original insurers to gain access to patient outcomes data (2) Create insurer-funded annuity fund to cover-out years if patient switches plans (3) Insurers and manufacturers work together with state regulators to implement policies that support alternative payment mechanisms

Source: Adapted from Alliance for Regenerative Medicine, Cook et al. 2018 IN VIVO

Over the long-term, payers expect the price of CAR-Ts to come down and be cheaper to administer

Long-Term CAR-T Expectations

Increased market competition expected to lower prices

Improvements in CAR-T manufacturing expected to lower COGS

Improved CAR-Ts safety

→ lower costs handling AEs
→ increased outpatient use
→ lower administrative cost

Commentary

"As more CAR-Ts are approved, I would expect prices to go down because then there is going to be aggressive price matching. As a rule of thumb, this starts to happen once four to five similar products launch"
– **Medical Director, National Plan**

"When these CAR-Ts mature and become more prevalent, the price is going to drop and it will become less costly to provide the service"
– **Medical Director, National Plan**

"A significant portion of CAR-T cases are expected to transition to the outpatient setting over time as refinements are made to products and to the clinical protocols aiming to predict and mitigate post-infusion complications"
– ASBMT + ASH Proposed CAR-T coverage and payment options (Nov, 2018)

Source: groupH research and analysis

Future products will need strong differentiation for commercial success when payers expect to manage the category more closely

1. **Multiple Approved CAR-T Products**
2. **Real World Experience** (*Outcomes, Cost Range*)
3. **More Aggressive Payer Management** (*Preferred CAR-T*)

- The combination of having multiple CAR-T products (especially those with overlapping indications) & real world experience in terms long term clinical outcomes and total cost of care including managing side effects will give payers the strong consideration to drive formulary product preference
- If outcomes between CAR-T products in the same indication are equal, several payers stated a cost differential range between 15%-30% would be enough to consider driving product preference or having a contract with a manufacturer to reimburse the payer for side effect management cases that fall out of the normal standard deviation

"If CAR-T's are similar in efficacy and the only difference is the side-effect profile, I think our contracting people may be interested in value-based contracts in terms of risk arrangements. If a manufacturer believes their product is safer, they will either pay for those ICU days or have some kind of rebate to equalize the cost in order to stay competitive"
Medical Director, National Plan

"If one CAR-T is dramatically safer and there is a cost offsets in addition to administering it in a less costly setting, we would create a step edit and require that product be tried first for that given condition. Safety comparisons are an important consideration as well as cost"
Medical Director, National Plan

Source: groupH research and analysis

groupH proposal #4: in the long term, groupH believes a blended annuity and risk sharing models will maximize value for all parties

Annuity Model

- Addresses budget impact when CAR-T's utilization increases
- Does not mitigate payer long-term value concerns

Risk-Sharing Model

- Mitigates payer uncertainty regarding outcomes
- By itself, does not affect budget impact

Blended Annuity & Risk-Sharing Model

- Blended models are very common in athletic sport contracts and very prevalent in Biopharma business development deals
- This model has the potential to be structured to appease all key stakeholders
- However, successful implementation will depend on ability to achieve industry consensus, favorable & consistent policy, and the devil will be in the 'details'

Source: groupH research and analysis

Several examples of Blended Annuity & Risk-Sharing models exist, from outside payer contracting

Illustrative Examples of 'Blended' Contract Structures

Sports Contract

American Football Contract

Signing Bonus: Similar to a patient copay or a limited acquisition cost to a provider to acquire the product

Base Salary: Similar to a yearly annuity payment

Risk-Share: If player gets arrested or suspended by the league, the player pays part of signing bonus / salary back to team, like a manufacturer paying back a payer for non-durable response

Performance Incentives: A player gets MVP, wins the championship – they get a bonus like a payer paying a drug maker for good outcomes

Biopharm BD Deal

M&A of a phase II asset

Upfront Payment: Similar to a patient copay or a limited acquisition cost to a provider to acquire the product. In a biopharma deal, this amount can vary from a high upfront to very little with payments back-ended with large milestones

Milestones Incentives: These are analogous to the pay-for-performance payments that payers pay drug makers. In a BD deal, these are the clinical, regulatory and commercial milestone payments

CAR-T Blended Model

Blended CAR-T Payments

Upfront Payment: This initial payment to manufacturer from a payer is to cover COGs to break even

Milestones: Milestones could be a small payment for 30 day response rate with a bonus payment for lack of intensive care for CRS. At 6 months of disease free survival & MRD, a larger payment is given with payments each year for disease free survival & MRD up to 3 years

Risk Share: Just as there are positive milestones, **failure of the product** or **excessive toxicities beyond an agreed upon standard** could also trigger back payments to payers

Source: groupH research and analysis

groupH, San Francisco

Morris Paterson
morris.paterson@groupH.com
m +1 415 969 1986

Michael Hy
michael.hy@groupH.com