Valoctocogene Roxaparvovec and Emicizumab for Hemophilia A without Inhibitors: Effectiveness and Value

Public Meeting — October 30, 2020

Meeting materials available at: https://icer-review.org/topic/hemophilia-a/
Donald Goldman, Person with Hemophilia

As a person with severe hemophilia who has survived to celebrate my 76th birthday on October 10, 2020, I can reflect on the advances in treatment over the past seven decades…. I have confidence that my great-grandchildren, if they have hemophilia, will benefit from miraculous treatment advances and perhaps even a cure.

Donald Goldman, Person with Hemophilia
Why Are We Here Today?

• What happens the day these treatments are approved by the FDA?
• What happens to patients and others in the health care “system”?
When There Isn’t Enough Money For Health Insurance

Gustavo Bendeck, Lubbock, Texas

The Whitmans, Bird City, Alaska

Luke Breen, Minneapolis, Minnesota
Organizational Overview

• The New England Comparative Effectiveness Public Advisory Council (CEPAC)

• The Institute for Clinical and Economic Review (ICER)
Sources of Funding, 2020
https://icer-review.org/about/support/

- Nonprofit Foundations: 70%
- Health Plans and Provider Group Contributions: 12%
- Manufacturer Contributions: 17%
- Other*: 1%

*Individual and matching contributions, government contracts, and speech stipends

ICER Policy Summit and non-report activities only
How Was the ICER Report Developed?

• Scoping with guidance from patient groups, clinical experts, manufacturers, and other stakeholders
• Internal ICER staff evidence analysis
• University of Illinois Chicago (UIC) cost-effectiveness modeling
• Public comment and revision
• Expert reviewers
  • Steven Pipe, MD, Professor of Pediatrics and Pathology Pediatric Medical Director, Hemophilia and Coagulation Disorders Program Director, University of Michigan
  • Margaret V. Ragni, MD, MPH, Professor of Medicine and Clinical and Translational Science, Medical Director of Hemophilia Center of Western PA, University of Pittsburgh Medical Center
  • Mark W. Skinner, JD, President & CEO, Institute for Policy Advancement Ltd.

• How is the evidence report structured to support New England CEPAC voting and policy discussion?
Fair Price, Fair Access, Future Innovation

Long-Term Value for Money

Short-Term Affordability
Health Benefits:
- Improved Function
- Longer Life
- Fewer Side Effects

Benefits Beyond Health and Special Social or Ethical Priorities

How Much Extra Should We Pay For The Better Health We Get?

Total Costs Including any Cost Savings from Better Health

Health Benefits: Improved Function

Health Benefits: Fewer Side Effects

Health Benefits: Longer Life
Consider Range of Pricing Linked to Better Health

Consider Benefits Beyond Health and Special Priorities

Price to reach $50k/QALY or evLYG

Price to reach $100k/QALY or evLYG

Price to reach $150k/QALY or evLYG

Maximum Price at Which We Can Do More Good Than Harm

Cost Effectiveness as a Part of Pricing to Value
## Agenda

<table>
<thead>
<tr>
<th>Time</th>
<th>Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>10:00 AM—10:20 AM</td>
<td>Meeting Convened and Opening Remarks</td>
</tr>
<tr>
<td></td>
<td>Steven D. Pearson, MD, MSc, President, ICER</td>
</tr>
<tr>
<td>10:20 AM—10:40 AM</td>
<td>Presentation of the Clinical Evidence</td>
</tr>
<tr>
<td></td>
<td>David Rind, MD, Chief Medical Officer, ICER</td>
</tr>
<tr>
<td>10:40 AM—11:10 AM</td>
<td>Presentation of the Economic Model</td>
</tr>
<tr>
<td></td>
<td>Surrey Walton, PhD, University of Illinois at Chicago College of Pharmacy</td>
</tr>
<tr>
<td>11:10 AM—11:20 AM</td>
<td>Break</td>
</tr>
<tr>
<td>11:20 AM—12:00 PM</td>
<td>Public Comments and Discussion</td>
</tr>
<tr>
<td>12:00 PM—12:40 PM</td>
<td>Lunch Break</td>
</tr>
<tr>
<td>12:40 PM—1:20 PM</td>
<td>New England CEPAC Vote on Clinical Effectiveness and Value</td>
</tr>
<tr>
<td>1:20 PM -- 1:30 PM</td>
<td>Break</td>
</tr>
<tr>
<td>1:30 PM—2:30 PM</td>
<td>Policy Roundtable</td>
</tr>
<tr>
<td>2:30 PM—3:00 PM</td>
<td>Reflections from New England CEPAC</td>
</tr>
<tr>
<td>3:00 PM</td>
<td>Meeting Adjourned</td>
</tr>
</tbody>
</table>
Clinical and Patient Experts

Brian O’Mahony, Chief Executive, Irish Haemophilia Society, Patient Advocate

- Brian O’Mahony has received fees for participation in advisory boards or educational activities from Bayer, BioMarin, Freeline, Roche and Uniqure.

Mark Skinner, JD, President & CEO, Institute for Policy Advancement Ltd, Patient Advocate

- Mr. Skinner has received fees and honoraria of more than $5,000 for educational presentations and advisory board participation from F. Hoffman-La Roche / Genentech, Bayer Healthcare, BioMarin, and the Blue Cross Blue Shield Association. Mr. Skinner’s household has or held equity interests in the following companies in the health sector: Cryosport, CVS Health, Editas Medicine, Horizon discovery, Illumina, Intellia Therapeutics, Intuitive Surgical, Johnson & Johnson (Sold), Novartis, Regeneron (Sold) and Teladoc Health. These holdings are independently managed by a financial advisor with instructions not to invest in companies with a known interest in therapies for bleeding disorders. Mr. Skinner is a member of the ICER Governing Board; Board of Directors of the World Federation of Hemophilia USA, which receives product and monetary donations for a global humanitarian aid program; serves as a consultant for the US National Hemophilia Foundation, and is a member of the NHF Scientific Advisory Council. Mr. Skinner is a Principal investigator for the Patient-Reported Outcomes and Burdens and Experiences (PROBE) study, which has received fees and grant support from Bayer, BioMarin, CSL-Behring, Freeline Therapeutics, Novo Nordisk, F. Hoffman-La Roche, Sanofi, Sobi, Takeda, uniQure. The PROBE study is an independent, investigator-led research project led by patients and patient advocacy organizations. Mr. Skinner is a person with severe hemophilia A.

Steven Pipe, MD, Pediatric Medical Director, Hemophilia and Coagulation Disorders Program, University of Michigan

- Dr. Steven Pipe has received consulting fees from Apcintex, Bayer, BioMarin, Catalyst Biosciences, CSL Behring, HEMA Biologics, Freeline, Novo Nordisk, Pfizer, Roche/Genentech, Sangamo Therapeutics, Sanofi, Takeda, Spark Therapeutics, uniQure.

Margaret Ragni, MD, MPH, Professor of Medicine and Clinical and Translational Medicine, University of Pittsburgh

- Dr. Margaret Ragni receives research funding (through the University of Pittsburgh) for gene therapy trials with SPARK, a gene therapy trial with BioMarin, and past gene therapy trial funding with Sangamo.
Key Collaborators

• Foluso Agboola, MBBS, MPH
• Serina Herron-Smith, BA
• Eric Borrelli, PharmD, MBA

Disclosures:

We have no conflicts of interest relevant to this report
Hemophilia A

• Deficiency in factor VIII
• Increased tendency to bleed
• X-linked recessive (1/5000 male births)
• Risk for life-threatening bleeding
• Bleeds into joints and muscles
• Joint bleeds lead to further bleeding and progressive joint damage
Prophylaxis

• Factor VIII for home treatment of bleeds became available in the 1970s

• Use of factor VIII infusions for prophylaxis became routine in severe hemophilia A by the early-to-mid 2000s

• Randomized trials demonstrated efficacy by the mid-to-late 2000s
Prophylaxis

• Burdensome
  • Factors are administered intravenously
  • Must be given frequently
  • Venous access can be difficult in young children
  • Elderly patients and those who develop arthropathy may find self-administration difficult
  • Adherence is a substantial problem
Potential Patient and Caregiver Restrictions

- Patient career
  - Bleeding risk
  - Near specialized care
  - Accessibility of factor
  - Flexible time

- Education
  - Near specialized care
  - Accessibility of factor
  - Flexible time

- Caregiver Career
  - Near specialized care
  - Flexible Time

- Location of Residence
  - Near specialized care
  - Accessibility of factor

- Recreation
  - Bleeding risk
  - Near specialized care
  - Accessibility of factor
Valoctocogene Roxaparvovec (Roctavian, BioMarin)

- “Valrox”
- AAV5 liver-directed gene therapy
- One-time administration to adults
- Complete Response Letter from FDA in August 2020
Emicizumab (Hemlibra®, Genentech)

- Bispecific antibody bridging aFIX and FX
- Subcutaneous injection every 1 to 4 weeks
- Used only for prophylaxis

- Approvals
  - Patients with inhibitors: 2017 (prior ICER review)
  - Patients without inhibitors: 2018
Scope of the Review

• **Population:** People with hemophilia A without inhibitors to factor VIII who would be appropriate for routine prophylaxis. For valoctocogene roxaparvovec, limited to adults.

• **Interventions:**
  - Gene therapy with valoctocogene roxaparvovec
  - Prophylaxis with emicizumab

• **Comparators:**
  - Prophylaxis with factor VIII
    - For valoctocogene roxaparvovec assessed benefit mainly by achieved factor levels
    - For emicizumab assessed benefit mainly by annualized bleed rates (ABRs)
  - Each other
Insights from Discussions with Patients

- Annualized bleeding rates do not adequately capture all aspects of the benefits, burdens, and harms of prophylaxis

- A curative therapy may be transformational in ways that even someone with hemophilia may not be able to understand before it happens

- Patients and patient groups have struggled to get insurance coverage for dosing regimens that maintain higher trough levels of factor VIII
Clinical Evidence
Valoctocogene Roxaparvovec

• Severity of Hemophilia
  • Severe: Factor VIII level < 1% of normal
  • Moderate: Factor VIII level 1% to 5% of normal
  • Mild: Factor VIII level 6% to 40% of normal

• Phase I/II open-label dose-finding trial (n = 15)
  • Primary endpoint of factor VIII activity ≥ 5 IU/dL
    • Achieved by 4 out of 5 patients who received $4 \times 10^{13}$ vg/kg
    • Achieved by 7 out of 7 patients who received $6 \times 10^{13}$ vg/kg
Valoctocogene Roxaparvovec

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Factor VIII Activity Over 4 Years in Cohort 3 of Phase I/II Study: One-Stage Assay

Factor VIII Activity Over 4 Years in Cohort 3 of Phase I/II Study: CS Assay
Year Four Severity (Chromogenic Assay)

- Non-hemophilic: 1
- Mild: 4
- Moderate: 1
- Severe: 1
Year Four Severity (One-Stage Assay)

- Non-hemophilic: 2
- Mild: 5
Other Information

• Mean ABR dropped from 16.3 to 0.8 after four years
• Years 2-4, 6 out of 7 patients had 0 bleeds (1/7 at baseline)
• Quality of life measures increased each year
• Most common adverse event was increase in liver enzymes
• All patients developed antibodies to AAV5
• Limited phase III data show only 7/16 achieved ≥40 IU/dL
Emicizumab

• HAVEN 3
  • Open label phase III RCT in patients without inhibitors
  • 89 patients not receiving prophylaxis: two dosing schedules of emicizumab versus no prophylaxis
  • (63 patients receiving prophylaxis, switched to emicizumab)

• SPINART
  • Open label RCT of factor VIII versus no prophylaxis in 84 patients
  • Standard half-life factor VIII dosed 25 IU/kg three times weekly
## NMA of Emicizumab vs. Factor VIII

**Annualized Treated Bleeds: Rate Ratio (95% Credible Interval)**

<table>
<thead>
<tr>
<th>Emicizumab</th>
<th>FVIII prophylaxis</th>
<th>On-demand FVIII</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.57 (0.22, 1.47)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.03 (0.02, 0.07)</td>
<td>0.06 (0.03, 0.11)</td>
<td></td>
</tr>
</tbody>
</table>

**Annualized Treated Joint Bleeds: Rate Ratio (95% Credible Interval)**

<table>
<thead>
<tr>
<th>Emicizumab</th>
<th>FVIII prophylaxis</th>
<th>On-demand FVIII</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.53 (0.2, 1.39)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0.03 (0.02, 0.07)</td>
<td>0.07 (0.03, 0.12)</td>
<td></td>
</tr>
</tbody>
</table>
Other Information

- RWE on bleeds in 39 children switching from FVIII to emicizumab
  - ABR decreased to 0.2 from 1.1
  - Zero bleeds in six months: 94% vs. 73%

- HAVEN 3
  - Non-statistically significant improvements in quality of life vs. no prophylaxis
  - Fewer missed days of work vs. no prophylaxis
  - In before/after study, 98% preferred emicizumab to FVIII prophylaxis

- Most common harms with emicizumab were injection site reactions
Valrox Uncertainties and Controversies

• Very few patients studied and reported on
• Interim phase III data appear to show lower success rates
• Factor levels declining over time
• Target cell is hepatocytes; factor VIII normally made in endothelial cells
Emicizumab Uncertainties and Controversies

- Effects on inhibitor development likely but unknown
- Best RCT evidence is against doses of factor VIII lower than typically used today in US
- RCT evidence may overestimate adherence to a burdensome therapy like factor VIII
Potential Other Benefits and Contextual Considerations

- Valoctocogene Roxaparvovec
  - Antibodies to AAV5
  - Even if limited duration of benefit, could allow period of time “cured”
  - Decreased burden/time of administering prophylaxis

- Emicizumab
  - Less burdensome administration (including for caregivers) and better adherence

- Both
  - Past iatrogenic harms
Public Comments Received

- B+ rating for emicizumab unreasonably high
- Inhibitor development
- Valoctocogene roxaparvovec bleeding rates
Summary: Valoctocogene Roxaparvovec vs. Factor VIII

• Marked improvements in many patients for a period of years
• Antibodies to AAV5 perhaps limiting better future treatments
• Potential long-term harms such as liver disease

• Promising but inconclusive (P/I)
Summary: Emicizumab vs. Factor VIII

• Emicizumab is superior to lower doses of factor VIII used in SPINART

• Uncertainties versus current doses of factor VIII

• Less burdensome and likely better adherence

• Thrombotic complications not seen in this population

• Comparable or better (C++)
Summary: Valoctocogene Roxaparvovec vs. Emicizumab

• Insufficient (I)
Questions?
Cost-Effectiveness

Surrey M Walton, PhD

Professor, Department of Pharmacy Systems Outcomes and Research

University of Illinois Chicago (UIC) College of Pharmacy
Key Review Team Members

Danny Quach, PharmD, PhD Student, Department of Pharmacy Systems Outcomes and Research

• University of Illinois Chicago

Disclosures:

Financial support was provided to the University of Illinois at Chicago from the Institute for Clinical and Economic Review.

The University of Illinois at Chicago researchers have no conflicts to disclose defined as more than $10,000 in health care company stock or more than $5,000 in honoraria or consultancies relevant to this report during the previous year from health care technology manufacturers or insurers.
Objectives

There were two primary objectives:

1) Estimate the life-time cost-effectiveness of valoctocogene roxaparvovec relative to prophylaxis with factor VIII in adult patients with severe hemophilia A and without inhibitors.

2) Estimate the life-time cost-effectiveness of emicizumab relative to prophylaxis with factor VIII in patients with hemophilia A suitable for factor VIII prophylaxis and without inhibitors.
Methods in Brief
Methods Overview Model 1

- **Model**: Semi-Markov Model
- **Setting**: United States
- **ICER Frameworks**: Ultra rare and Single/Short-term Transformative Therapy;
- **Perspective**: Health Care Sector Perspective
- **Time Horizon**: Lifetime
- **Discount Rate**: 3% per year (costs and outcomes)
- **Cycle Length**: 6 Months
- **Primary Outcome**: Cost per quality-adjusted life year (QALY) gained, cost per life year (LY) gained, cost per treated bleed avoided
Methods Overview Model 2

- **Model:** Semi-Markov Model
- **Setting:** United States
- **ICER Framework:** Standard
- **Perspective:** Health Care Sector Perspective
- **Time Horizon:** Lifetime
- **Discount Rate:** 3% per year (costs and outcomes)
- **Cycle Length:** 6 Months
- **Primary Outcome:** Cost per quality-adjusted life year (QALY) gained, cost per life year (LY) gained, cost per treated bleed avoided
Model Schematic

- Emicizumab
- Factor VIII

States:
- No Arthropathy (PS = 0)
- Arthropathy (PS = 1, 2, 27)
- Joint Replacement Surgery (PS = 28)
- Dead

Transitions:
- Emicizumab to No Arthropathy
- Factor VIII to No Arthropathy
- Arthropathy to Dead
- Arthropathy to Joint Replacement Surgery
- Arthropathy to Arthropathy (PS = 1, 2, 27)
- Joint Replacement Surgery to Dead
Key Model Assumptions

• Model 1 bleed rates for valoctocogene roxaparvovec were based on projected factor levels and literature-based estimates of bleed rates across factor levels.

• In Model 1, at projected factor levels below 5%, 5% of patients are assumed to switch to emicizumab prophylaxis. At projected factor levels below 1%, all patients were assumed to switch to emicizumab.

• Bleed rates for emicizumab are taken from the Haven 3 trial.

• Bleed rates for factor VIII are from a recent published study by Malec et. al. examining bleed rates in US hemophilia treatment centers affiliated with the American Thrombosis & Hemostasis Network (ATHN).
  • We view the factor VIII rates as an evidence based lower bound for bleeds associated with current dosing.
Key Model Assumptions

• Proportions of bleed types relative to treated bleeds in the HAVEN 3 trial were used to estimate different types of bleeds relative to treated bleeds for factor VIII and valoctocogene roxaparvovec.

  • An average proportion of all bleeds that are joint bleeds in the HAVEN 3 and POTTER trials determined joint bleeds relative to total bleeds.

• Factor VIII costs are based on two representative treatments, Advate for standard half-life, and Eloctate for extended half-life, using doses and proportions of patients on those drugs consistent with patients treated with those treatments in US hemophilia treatment centers affiliated with ATHN.
Key Model Assumptions

• The utilities associated with a bleed are applied fully for two days and an average of the no bleed and bleed values for the remainder of a week.

• Cost per treated bleeds are the same for all comparators.

• Patient weights and mortality rates were based on US male population averages.

• There were no mortality effects for any treatment.
Starting Points and Transitions

• In Model 1 patients start with a PS of 13. In model 2 they start with a PS of 0.

• PS transition rates are consistent with a 1-point increase for every 36.52 bleeds for patients under 25 and for every 6.52 joint bleeds over the age of 25.

• At a PS score of 28, patients have surgery and return to a PS of 1.
## Key Model Inputs: Bleed Rates

<table>
<thead>
<tr>
<th>Drug</th>
<th>All Bleeds</th>
<th>All Joint Bleeds</th>
<th>Non-Target Joint Bleeds (Treated)</th>
<th>Target Joint Bleeds (Treated)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Factor VIII</td>
<td>2.60</td>
<td>1.72</td>
<td>0.60</td>
<td>0.70</td>
</tr>
<tr>
<td>Emicizumab</td>
<td>2.60</td>
<td>1.72</td>
<td>0.60</td>
<td>0.70</td>
</tr>
<tr>
<td>Valoctocogene Roxaparvovec Year 2</td>
<td>0.45</td>
<td>0.30</td>
<td>0.10</td>
<td>0.12</td>
</tr>
<tr>
<td>Valoctocogene Roxaparvovec Year 10</td>
<td>7.05</td>
<td>4.65</td>
<td>1.63</td>
<td>1.90</td>
</tr>
<tr>
<td>Valoctocogene Roxaparvovec Year 13</td>
<td>2.60</td>
<td>1.72</td>
<td>0.60</td>
<td>0.70</td>
</tr>
</tbody>
</table>

*Includes treated and untreated bleeds*
Key Model Inputs: Health State Utilities

<table>
<thead>
<tr>
<th>Age</th>
<th>Pettersson 0</th>
<th>Pettersson 1-27</th>
<th>Surgery</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-30</td>
<td>0.94</td>
<td>0.82</td>
<td>0.72</td>
<td>O'Hara 2018; Laupacis 1993</td>
</tr>
<tr>
<td>31-40</td>
<td>0.84</td>
<td>0.74</td>
<td>0.65</td>
<td>O'Hara 2018; Laupacis 1993</td>
</tr>
<tr>
<td>41-50</td>
<td>0.86</td>
<td>0.69</td>
<td>0.61</td>
<td>O'Hara 2018; Laupacis 1993</td>
</tr>
<tr>
<td>51-60</td>
<td>0.83</td>
<td>0.63</td>
<td>0.56</td>
<td>O'Hara 2018; Laupacis 1993</td>
</tr>
<tr>
<td>61-100</td>
<td>0.73</td>
<td>0.54</td>
<td>0.48</td>
<td>O'Hara 2018; Laupacis 1993</td>
</tr>
</tbody>
</table>

Utilities are based on EQ-5D surveys completed by hemophilia patients in Europe. The surgery utility is a time trade off score from patients pre hip surgery. The utility of surgery is based on one month of a utility of 0.32, and 5 months at a utility corresponding to a Pettersson score of 1-27.
Key Model Inputs: Utilities

<table>
<thead>
<tr>
<th>Bleed Disutilities</th>
<th>Value/Bleed/Cycle</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bleed Not Into A Target Joint</td>
<td>-0.002</td>
<td>Neufeld 2012</td>
</tr>
<tr>
<td>Target Joint Bleed</td>
<td>-0.003</td>
<td>Mazza 2016</td>
</tr>
</tbody>
</table>

These are based on a -0.16 and -0.28 disutility per day for treated bleed and treated joint bleed. EQ-5D based utilities by patients or caregivers.
## Key Model Inputs: Drug Regimens

<table>
<thead>
<tr>
<th>Generic name</th>
<th>Drug A</th>
<th>Drug B</th>
<th>Drug C</th>
<th>Drug C</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brand Name</td>
<td>Hemlibra®</td>
<td>Roctavian™</td>
<td>Advate®</td>
<td>Eloctate®</td>
</tr>
<tr>
<td>Generic Name</td>
<td>Emicizumab</td>
<td>Valoctocogene roxaparvovec</td>
<td>Antihemophilic factor (recombinant)</td>
<td>Antihemophilic factor (recombinant), Fc fusion protein</td>
</tr>
<tr>
<td>Manufacturer</td>
<td>Genentech</td>
<td>BioMarin</td>
<td>Baxter</td>
<td>Biogen</td>
</tr>
<tr>
<td>Route of Administration</td>
<td>subcutaneous</td>
<td>IV</td>
<td>IV</td>
<td>IV</td>
</tr>
<tr>
<td>Dosing</td>
<td>3mg/kg every week for the first month and then 3 mg/kg every 2 weeks after</td>
<td>$6 \times 10^{13}$ vg/kg</td>
<td>118.2 IU/kg every week</td>
<td>111.2 IU/kg every week</td>
</tr>
</tbody>
</table>

For Factor VIII, 71.18% take Advate and 28.82% take Eloctate. For all bleeds, the same basket and a 54 IU/kg dose of each drug was used. We recognize dosing regimens vary widely in practice.
### Key Model Inputs: Treatment Costs

<table>
<thead>
<tr>
<th>Drug</th>
<th>WAC per Dose</th>
<th>Discount from WAC</th>
<th>Add-On Discount</th>
<th>Net Price per Dose</th>
<th>Net Price per Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Valoctocogene roxaparvovec (Roctavian™)</td>
<td>$2,500,000</td>
<td>--</td>
<td>0%</td>
<td>$2,500,000</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Emicizumab (Hemlibra®)</td>
<td>$100.19/mg</td>
<td>4.7%</td>
<td>6%</td>
<td>$89.33/mg</td>
<td>$569,105</td>
</tr>
<tr>
<td>Antihemophilic Factor (recombinant) (Advate®)</td>
<td>$1.69/IU</td>
<td>18.6%</td>
<td>6%</td>
<td>$1.08/IU</td>
<td>$542,539</td>
</tr>
<tr>
<td>Antihemophilic Factor, Fc fusion protein (Eloctate®)</td>
<td>$2.23/IU</td>
<td>3.2%</td>
<td>6%</td>
<td>$1.82/IU</td>
<td>$858,026</td>
</tr>
</tbody>
</table>

These all vary by weight and are shown for an 81.4 Kg patient. The average cost of Factor VIII is $633,462. The average treatment cost per bleed was $5,275 for an 81.4kg male.
## Key Model Inputs: Non-Drug Costs per Bleed

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Cost</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 18</td>
<td>$765.48</td>
<td>Shrestha 2017</td>
</tr>
<tr>
<td>18-45</td>
<td>$4,604.32</td>
<td>Shrestha 2017</td>
</tr>
<tr>
<td>&gt; 45</td>
<td>$6,858.24</td>
<td>Shrestha 2017</td>
</tr>
</tbody>
</table>

Additional societal costs per bleed were $1,162
## Key Model Inputs: Other Costs

<table>
<thead>
<tr>
<th></th>
<th>Annual Cost</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>No Arthropathy</strong></td>
<td>$354.20 per cycle based on office visits and joint related tests</td>
<td>O'Hara 2018 and CMS Fees</td>
</tr>
<tr>
<td><strong>Arthropathy</strong></td>
<td>$618.28 per cycle based on office visits and joint related tests</td>
<td>O'Hara 2018 and CMS Fees</td>
</tr>
<tr>
<td><strong>Surgery</strong></td>
<td>Arthropathy plus $44,717.17*</td>
<td>Earnshaw 2015</td>
</tr>
</tbody>
</table>

*The cost of surgery was derived from Earnshaw et al., which reported a surgery cost of $44,717.17 when inflated to 2019 dollars*
Results
## Base-Case Results Model 1

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Drug Cost</th>
<th>Total Cost</th>
<th>Infusions</th>
<th>Joint Bleeds</th>
<th>Treated Non-Target Joint Bleeds</th>
<th>Treated Target Joint Bleeds</th>
<th>Life Years</th>
<th>QALYs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Factor VIII (Model 1 – Health Sector Perspective)</td>
<td>$18,269,000</td>
<td>$18,722,000</td>
<td>3705.17</td>
<td>68.97</td>
<td>15.92</td>
<td>18.57</td>
<td>26.53</td>
<td>19.087</td>
</tr>
<tr>
<td>Valoctocogene Roxaparvovec (Model 1 – Health Sector Perspective)</td>
<td>$13,293,000</td>
<td>$13,693,000</td>
<td>31.11</td>
<td>43.70</td>
<td>15.28</td>
<td>17.83</td>
<td>26.53</td>
<td>19.091</td>
</tr>
</tbody>
</table>

QALYs: quality-adjusted life years
## Base-Case Incremental Results Model 1

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Incremental Cost</th>
<th>Incremental QALYs</th>
<th>Incremental Cost-Effectiveness Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Valoctocogene Roxaparvovec vs. Factor VIII (Model 1 – Health Sector Perspective)</td>
<td>-$4,988,000</td>
<td>0.004</td>
<td>Dominant</td>
</tr>
</tbody>
</table>

QALY: quality-adjusted life year
### Base-Case Results Model 2

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Drug Cost</th>
<th>Total Cost</th>
<th>Infusions</th>
<th>Joint Bleeds</th>
<th>Treated Non-Target Joint Bleeds</th>
<th>Treated Target Joint Bleeds</th>
<th>Life Years</th>
<th>QALYs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Factor VIII (Model 2 – Health Sector Perspective)</td>
<td>$14,821,000</td>
<td>$15,104,000</td>
<td>4058.67</td>
<td>38.60</td>
<td>12.64</td>
<td>13.76</td>
<td>29.14</td>
<td>24.141</td>
</tr>
<tr>
<td>Emicizumab (Model 2 – Health Sector Perspective)</td>
<td>$13,316,000</td>
<td>$13,598,000</td>
<td>26.41</td>
<td>38.60</td>
<td>12.64</td>
<td>13.76</td>
<td>29.14</td>
<td>24.141</td>
</tr>
</tbody>
</table>

QALYs: quality-adjusted life years
## Base-Case Incremental Results Model 2

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Incremental Cost</th>
<th>Incremental QALYs</th>
<th>Incremental Cost-Effectiveness Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Emicizumab vs Factor VIII (Model 2 – Health Sector Perspective)</td>
<td>-$1,505,000</td>
<td>0.000</td>
<td>Cost Saving</td>
</tr>
</tbody>
</table>

QALY: quality-adjusted life year
One Way Sensitivity Analyses - Model 1

Model 1 - Health Sector - Valrox Incremental Costs

Model 1 - Valrox Incremental QALYs

- Factor VIII Total Treated Bleeds
  - Low Input Value: 0.98
  - High Input Value: 1.63

- Emicizumab Total Treated Bleeds
  - Low Input Value: 0.98
  - High Input Value: 1.63

- Valacogogene Treated Joint Bleed RR
  - Low Input Value: 0.09
  - High Input Value: 0.30

- Average Number of Blood Days
  - Low Input Value: 1.00
  - High Input Value: 7.00

- Pettersson 13-21 Utilities (Age > 60)
  - Low Input Value: 0.41
  - High Input Value: 0.68

- Pettersson 22-28 Utilities (Age > 60)
  - Low Input Value: 0.41
  - High Input Value: 0.68

- Pettersson 13-21 Utilities (30 < Age ≤ 40)
  - Low Input Value: 0.56
  - High Input Value: 0.93

- Pettersson 22-28 Utilities (30 < Age ≤ 40)
  - Low Input Value: 0.56
  - High Input Value: 0.93

- Pettersson 13-21 Utilities (50 < Age ≤ 60)
  - Low Input Value: 0.47
  - High Input Value: 0.79

- Pettersson 22-28 Utilities (50 < Age ≤ 60)
  - Low Input Value: 0.47
  - High Input Value: 0.79
One Way Sensitivity Analyses - Model 2

Model version 2 - Emicizumab
Incremental Costs

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Low Input Value</th>
<th>High Input Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Emicizumab Net Drug Cost</td>
<td>$71.27</td>
<td>$118.79</td>
</tr>
<tr>
<td>Emicizumab (Month 2+) Prophylaxis Drug Dosing</td>
<td>1.13</td>
<td>1.88</td>
</tr>
<tr>
<td>Advate (F8) Net Drug Cost</td>
<td>$0.86</td>
<td>$1.44</td>
</tr>
<tr>
<td>Advate (F8) Prophylaxis Drug Dosing</td>
<td>88.65</td>
<td>147.75</td>
</tr>
<tr>
<td>Eloctate (F8) Net Drug Cost</td>
<td>$1.45</td>
<td>$2.42</td>
</tr>
<tr>
<td>Eloctate (F8) Prophylaxis Drug Dosing</td>
<td>83.40</td>
<td>130.00</td>
</tr>
<tr>
<td>Emicizumab Furnishing Discount (%)</td>
<td>4.50%</td>
<td>7.50%</td>
</tr>
<tr>
<td>Advate (F8) Furnishing Discount (%)</td>
<td>4.50%</td>
<td>7.50%</td>
</tr>
<tr>
<td>Eloctate (F8) Furnishing Discount (%)</td>
<td>0.05</td>
<td>0.08</td>
</tr>
<tr>
<td>Factor VIII Total Treated Bleeds</td>
<td>97.50%</td>
<td>162.50%</td>
</tr>
</tbody>
</table>

Model version 2 - Emicizumab
Incremental QALYs

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Low Input Value</th>
<th>High Input Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Factor VIII Total Treated Bleeds</td>
<td>0.98</td>
<td>1.63</td>
</tr>
<tr>
<td>Emicizumab Total Treated Bleeds</td>
<td>0.98</td>
<td>1.63</td>
</tr>
</tbody>
</table>

Low Input Value
High Input Value
## Probabilistic Sensitivity Analysis Model 1

<table>
<thead>
<tr>
<th></th>
<th>Cost Effective at $50,000 per QALY</th>
<th>Cost Effective at $100,000 per QALY</th>
<th>Cost Effective at $150,000 per QALY</th>
<th>Cost Effective at $200,000 per QALY</th>
<th>Cost Effective at $250,000 per QALY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Valoctocogene Roxaparvovec (Model 1 – Health Sector Perspective)</td>
<td>93.92%</td>
<td>93.93%</td>
<td>93.93%</td>
<td>93.93%</td>
<td>93.93%</td>
</tr>
</tbody>
</table>

Results use a placeholder price of $2,500,000 for valoctocogene roxaparvovec
# Probabilistic Sensitivity Analysis Model 2

<table>
<thead>
<tr>
<th></th>
<th>Cost Effective at $50,000 per QALY</th>
<th>Cost Effective at $100,000 per QALY</th>
<th>Cost Effective at $150,000 per QALY</th>
<th>Cost Effective at $200,000 per QALY</th>
<th>Cost Effective at $250,000 per QALY</th>
</tr>
</thead>
<tbody>
<tr>
<td>Emicizumab (Model 2)</td>
<td>69.43%</td>
<td>69.43%</td>
<td>69.42%</td>
<td>69.46%</td>
<td>60.47%</td>
</tr>
</tbody>
</table>

QALY: quality-adjusted life year
Scenario Analyses

- Using higher bleed durations, higher bleed rates, an older starting age in model 1, surgery return to PS score of 13, and societal perspectives had very little impact on the results.

- In the SST scenarios for model 1, the conservative and optimistic duration scenarios as well as a proposed payment scenario all resulted in valoctocogene roxaparvovec being dominant.
## Limited Savings SST Scenario Analyses Model 1

<table>
<thead>
<tr>
<th>Scenario</th>
<th>Treatment</th>
<th>Incremental Cost</th>
<th>Incremental QALYs</th>
<th>Incremental Cost-Effectiveness Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Half Savings During Treatment</td>
<td>Valoctocogene Roxaparvovec</td>
<td>-$666,000</td>
<td>0.004</td>
<td>Dominant</td>
</tr>
<tr>
<td>Cap Savings at $150,000/Year During Treatment</td>
<td>Valoctocogene Roxaparvovec</td>
<td>$923,000</td>
<td>0.004</td>
<td>$230,750,000/QALY</td>
</tr>
</tbody>
</table>

*The incremental costs were the same in the societal and health sector scenarios only after rounding to the nearest $1000.*
# NMA Scenario Analyses Model 1

<table>
<thead>
<tr>
<th>Treatment (Perspective)</th>
<th>Incremental Cost</th>
<th>Incremental QALYs</th>
<th>Incremental Cost-Effectiveness Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Valoctocogene Roxaparvovec (Health Sector Perspective)</td>
<td>$452,000</td>
<td>0.076</td>
<td>$5,949,000/QALY gained</td>
</tr>
</tbody>
</table>

Results use a placeholder price of $2,500,000 for valoctocogene roxaparvovec
NMA Scenario Analysis Model 2

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Incremental Cost</th>
<th>Incremental QALYs</th>
<th>Incremental Cost-Effectiveness Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Emicizumab</td>
<td>$2,948,000</td>
<td>0.284</td>
<td>$10,393,000/QALY gained</td>
</tr>
</tbody>
</table>
Limitations

- Both models are based on limited data particularly for valoctocogene roxaparvovec.

- The models do not include adherence.

- Dosing for Factor VIII was from US hemophilia centers while those for emicizumab and valoctocogene roxaparvovec were from clinical trials.

- We also did not incorporate inhibitor development into model 2 as we received conflicting clinical opinion about which regimen would lead to more inhibitor development and it has already been shown that emicizumab is a dominant treatment for patients with inhibitors.
Limitations

• The relationship between joint bleeds and surgery is imperfect and the model assumes one joint requiring surgery at a time. This may undercount surgeries overall. To help address this, we examined the impact of varying some of the model assumptions around surgery and the impact was small.

• Utility scores for bleeds came from patients with inhibitors and these may be different in patients without inhibitors.

• We are using a placeholder price for valoctocogene roxaparvovec.

• We use Advate and Eloctate as representative treatments and average doses from ATHN data. There are numerous other factor VIII products on the market and a wide variance of treatment regimens.

  • The results here would not directly apply to those products and as shown in the sensitivity and scenario analyses variation in dosing can have major implications on the projected cost effectiveness of factor VIII.
Comments Received

• Lots of comments that dosing should not be based on one trial for factor VIII which prompted changing the base case from being based on the NMA to being based on doses in the ATHN data set.

• Several other comments on dosing as well as use of other factor VIII products.
  • We recognize the variance in treatment and that dosing is a KEY variable.

• Using a pharmacokinetic based model around dosing.
  • Theoretically this should mimic the average dose we used but could impact the variance.

• Accounting for treatment burden of factor VIII in the model.
  • We did not find high quality inputs for this, but we do report the number of infusions.
Conclusions

• With representative doses and a data driven upper bound on efficacy for factor VIII, and using a placeholder price of $2.5 million, valoctocogene roxaparvovec was found to be a dominant treatment for adult patients with hemophilia A without inhibitors.

• With representative doses and a data driven upper bound on efficacy for factor VIII, emicizumab was found to be a highly cost saving treatment with equal efficacy to factor VIII.

• These results depend heavily on the high costs of factor VIII products.
Questions?
Break

Meeting will resume at 11:31am ET
Manufacturer Public Comment and Discussion
Richard Ko, MD, MHS, MS
Head of Rare Blood Disorders, US Medical Affairs, Genentech, Inc.

Conflicts of Interest:

- *Dr. Richard Ko is a full-time employee of Genentech, Inc.*
Caution: This information is for educational purposes only and should not be used as a substitute for professional medical advice. Always consult a healthcare provider for individual advice regarding a medical condition.

Bob G. Schultz, PharmD, MS, Senior Manager – Outcome Research
Takeda Pharmaceuticals, Inc.

Conflicts of Interest:

• Dr. Bob Shultz is a full-time employee of Takeda Pharmaceuticals, Inc.
Conflicts of Interest:

• Dr. Parth Vashi is a full-time employee of Bayer.
Conflicts of Interest:

- Dr. Wing Yen Wong is a full-time employee of BioMarin.
Public Comment and Discussion
Len Valentino, MD, President & Chief Executive Officer, National Hemophilia Foundation

Conflicts of Interest:

- The National Hemophilia Foundation is a 501c3 organization that receives program and educational grant funding from manufacturers of hemophilia products to support their mission.
Sonji Wilkes, Senior Director, Policy, Advocacy & Government Education, Hemophilia Federation of America

Conflicts of Interest:

• Hemophilia Federation of America receives manufacturer support, consulting fees and honoraria from Takeda, Genentech, Bayer, CSL Behring, Novo Nordisk, Sanofi Genzyme, HEMA Biologics, Kedrion BioPharma, Pfizer, Aptevo, BioMarin, Grifols, Octapharma, Spark Therapeutics, UniQure, Siaglon Therapeutics, PCORI.
Conflicts of Interest:

• No financial conflicts to disclose.
Ryan Hallock, LPN, Patient Advocate

Conflicts of Interest:

- Ryan Hallock is a Board Member for the Mississippi Hemophilia Foundation.
Jennifer Sleboda, Patient Advocate

Conflicts of Interest:

• Jennifer Sleboda is a Board Member of the Hemophilia Association of the Capital Area, which receives funding from pharmaceutical and home care companies.
Lunch

Meeting will resume at 1pm ET
Voting Questions
1. For patients with hemophilia A without inhibitors to factor VIII, is the evidence adequate to demonstrate that the net health benefit of emicizumab (Hemlibra, Genentech) is superior to that provided by prophylaxis with factor VIII?

A. Yes

B. No
2. Please vote 1, 2, or 3 on the following potential other benefits and contextual considerations as they relate to emicizumab.

A. 1

B. 2

C. 3
2a. Please vote 1, 2, or 3 on the following potential other benefits and contextual considerations as they relate to emicizumab.

A. 1

B. 2

C. 3
2b. Please vote 1, 2, or 3 on the following potential other benefits and contextual considerations as they relate to emicizumab.

A. 1
B. 2
C. 3

<table>
<thead>
<tr>
<th>Likert Scale of Potential Other Benefits and Contextual Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (Suggests Lower Value)</td>
</tr>
<tr>
<td>Very similar mechanism of action to that of other active treatments.</td>
</tr>
</tbody>
</table>
2c. Please vote 1, 2, or 3 on the following potential other benefits and contextual considerations as they relate to emicizumab.

A. 1

B. 2

C. 3

<table>
<thead>
<tr>
<th>Likert Scale of Potential Other Benefits and Contextual Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (Suggests Lower Value)</td>
</tr>
<tr>
<td>Delivery mechanism or relative complexity of regimen likely to lead to much lower real-world adherence and worse outcomes relative to an active comparator than estimated from clinical trials.</td>
</tr>
</tbody>
</table>
2d. Please vote 1, 2, or 3 on the following potential other benefits and contextual considerations as they relate to emicizumab.

A. 1
B. 2
C. 3

<table>
<thead>
<tr>
<th>Likert Scale of Potential Other Benefits and Contextual Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (Suggests Lower Value)</td>
</tr>
<tr>
<td>This intervention could reduce or preclude the potential effectiveness of future treatments.</td>
</tr>
</tbody>
</table>
2e. Please vote 1, 2, or 3 on the following potential other benefits and contextual considerations as they relate to emicizumab.

A. 1

B. 2

C. 3

<table>
<thead>
<tr>
<th>Likert Scale of Potential Other Benefits and Contextual Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (Suggests Lower Value)</td>
</tr>
<tr>
<td>2 (Intermediate)</td>
</tr>
<tr>
<td>3 (Suggests Higher Value)</td>
</tr>
</tbody>
</table>

The intervention offers no special advantages to patients by virtue of presenting an option with a notably different balance or timing of risks and benefits.

The intervention offers special advantages to patients by virtue of presenting an option with a notably different balance or timing of risks and benefits.
2f. Please vote 1, 2, or 3 on the following potential other benefits and contextual considerations as they relate to emicizumab.

A. 1
B. 2
C. 3
2g. Please vote 1, 2, or 3 on the following potential other benefits and contextual considerations as they relate to emicizumab.

A. 1

B. 2

C. 3

<table>
<thead>
<tr>
<th>Likert Scale of Potential Other Benefits and Contextual Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (Suggests Lower Value)</td>
</tr>
<tr>
<td>Small health loss without this treatment as measured by absolute QALY shortfall.</td>
</tr>
</tbody>
</table>
2h. Please vote 1, 2, or 3 on the following potential other benefits and contextual considerations as they relate to emicizumab.

A. 1
B. 2
C. 3

<table>
<thead>
<tr>
<th>Likert Scale of Potential Other Benefits and Contextual Considerations</th>
<th>1 (Suggests Lower Value)</th>
<th>2 (Intermediate)</th>
<th>3 (Suggests Higher Value)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Small health loss without this treatment as measured by proportional QALY shortfall.</td>
<td></td>
<td></td>
<td>Substantial health loss without this treatment as measured by proportional QALY shortfall.</td>
</tr>
</tbody>
</table>
2i. Please vote 1, 2, or 3 on the following potential other benefits and contextual considerations as they relate to emicizumab.

A. 1
B. 2
C. 3
2j. Please vote 1, 2, or 3 on the following potential other benefits and contextual considerations as they relate to emicizumab.

A. 1
B. 2
C. 3

<table>
<thead>
<tr>
<th>Likert Scale of Potential Other Benefits and Contextual Considerations</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (Suggests Lower Value)</td>
</tr>
<tr>
<td>2 (Intermediate)</td>
</tr>
<tr>
<td>3 (Suggests Higher Value)</td>
</tr>
<tr>
<td>Will not have a significant impact on improving return to work and/or overall productivity vs. the comparator.</td>
</tr>
<tr>
<td>Will have a significant impact on improving return to work and/or overall productivity vs. the comparator.</td>
</tr>
</tbody>
</table>
2k. Please vote 1, 2, or 3 on the following potential other benefits and contextual considerations as they relate to emicizumab.

A. 1
B. 2
C. 3
Break

Meeting will resume at 1:50pm ET
Policy Roundtable
## Policy Roundtable

<table>
<thead>
<tr>
<th>Policy Roundtable Participant</th>
<th>Conflict of Interest</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leslie Fish, RPh, PharmD, Vice President of Clinical Pharmacy, IDP Analytics</td>
<td>No financial conflicts to disclose.</td>
</tr>
<tr>
<td>Richard Ko, MD, MHS, MS, Head of Rare Blood Disorders, US Medical Affairs, Genentech, Inc.</td>
<td>Dr. Richard Ko is a full-time employee of Genentech, Inc.</td>
</tr>
<tr>
<td>Brian O’Mahony, Chief Executive, Irish Haemophilia Society, Patient Advocate</td>
<td>Brian O’Mahony has received fees for participation in advisory boards or educational activities from Bayer, BioMarin, Freeline, Roche and Uniqure.</td>
</tr>
<tr>
<td>Steven Pipe, MD, Pediatric Medical Director, Hemophilia and Coagulation Disorders Program, University of Michigan</td>
<td>Dr. Steven Pipe has received consulting fees from Apicintex, Bayer, BioMarin, Catalyst Biosciences, CSL Behring, HEMA Biologics, Freeline, Novo Nordisk, Pfizer, Roche/Genentech, Sangamo Therapeutics, Sanofi, Takeda, Spark Therapeutics, uniQure.</td>
</tr>
<tr>
<td>Margaret Ragni, MD, MPH, Professor of Medicine and Clinical and Translational Medicine, University of Pittsburgh</td>
<td>Dr. Margaret Ragni receives research funding (through the University of Pittsburgh) for gene therapy trials with SPARK, a gene therapy trial with BioMarin, and past gene therapy trial funding with Sangamo.</td>
</tr>
<tr>
<td>Mark Skinner, JD, President &amp; CEO, Institute for Policy Advancement Ltd, Patient Advocate</td>
<td>*</td>
</tr>
<tr>
<td>Wing Yen Wong, MD, Group Vice President, Global Medical Affairs, BioMarin Pharmaceutical Inc</td>
<td>Dr. Wing Yen Wong is a full-time employee of BioMarin Pharmaceuticals.</td>
</tr>
<tr>
<td>John Watkins, PharmD, MPH, BCPS Formulary Manager, Premera Blue Cross</td>
<td>Dr. John Watkins is a full-time employee of Premera Blue Cross.</td>
</tr>
<tr>
<td>Todd Williamson, PhD, MSc, Vice President, Data Generation &amp; Observational Studies, Bayer</td>
<td>Dr. Todd Williamson is a full-time employee of Bayer Pharmaceuticals.</td>
</tr>
</tbody>
</table>

*Please refer to Clinical and Patient Expert slide for conflicts of interest.
New England CEPAC Council Reflections
Next Steps

• Meeting recording posted to ICER website next week

• Final Report published on or around November 20, 2020
  • Includes description of New England votes, deliberation, policy roundtable discussion

• Materials available at: https://icer-review.org/topic/hemophilia-a/
Adjourn