Building Beyond Hepatitis B/D:

HSV-2 & Transplant-Associated Herpesviruses

Aug 31, 2022

Nasdaq: ASMB

Agenda

- Applying unparalleled expertise in virologic drug development to expand Assembly Bio's portfolio into new viral diseases
  - John McHutchison AO, MD, Chief Executive Officer at Assembly Bio
- Assembly Bio's differentiated antiviral approach for HSV-2 and an early look at the program for transplant-associated herpesvirus infections
  - William Delaney, PhD, Chief Scientific Officer at Assembly Bio
- Q&A with Sir Michael Houghton, PhD
- Update on 2022 Progress
  - John McHutchison

Today's Speakers

John McHutchison AO, MD

Chief Executive Officer

William Delaney, PhD

Chief Scientific Officer

Sir Michael Houghton, PhD

Director, Li Ka Shing Applied Virology Institute, University of Alberta, Edmonton, Canada

Cautionary Note Regarding Forward-Looking Statements

The information in this presentation contains forward-looking statements that are subject to certain risks and uncertainties that could cause actual results to materially differ. These risks and uncertainties include: Assembly Bio's ability to successfully execute its previously announced reprioritization and restructuring activities; potential adverse legal, reputational, operational and financial effects on Assembly Bio resulting from the reprioritization and restructuring activities; Assembly Bio's ability to initiate and complete clinical studies involving its therapeutic product candidates, including studies contemplated by Assembly Bio's collaboration agreements, in the currently anticipated timeframes; safety and efficacy data from clinical studies may not warrant further development of Assembly Bio's product candidates; clinical and nonclinical data presented at conferences may not differentiate Assembly Bio's product candidates from other companies' candidates; results of nonclinical studies may not be representative of disease behavior in a clinical setting and may not be predictive of the outcomes of clinical studies; continued development and commercialization of ABI-H3733, if successful, in the China territory will be dependent on, and subject to, Assembly Bio's collaboration agreement governing this activity in the China territory; Assembly Bio's ability to maintain financial resources necessary to continue its clinical studies and fund business operations; any impact that the COVID-19 pandemic may have on Assembly Bio's business and operations, including initiation, enrollment and continuation of its clinical studies or timing of discussions with regulatory authorities; and other risks identified from time to time in Assembly Bio's reports filed with the U.S. Securities and Exchange Commission (the SEC). You are urged to consider statements that include the words may, will, would, could, should, might, believes, hopes, estimates, projects, potential, expects, plans, anticipates, intends, continues, forecast, designed, goal or the negative of those words or other comparable words to be uncertain and forward-looking. Assembly Bio intends such forward-looking statements to be covered by the safe harbor provisions contained in Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. More information about Assembly Bio's risks and uncertainties are more fully detailed under the heading "Risk Factors" in Assembly Bio's filings with the SEC, including its most recent Annual Report on Form 10-K, Quarterly Reports on Form 10-Q and Current Reports on Form 8-K. Except as required by law, Assembly Bio assumes no obligation to update publicly any forward-looking statements, whether as a result of new information, future events or otherwise.

Advancing a Clinical & Research Stage Portfolio of Small Molecules for HBV and Other Viral Diseases

*While Assembly Bio has discontinued further development of first-generation core inhibitor, vebicorvir (VBR), a Phase 2 triple combination study conducted in collaboration with Arbutus Biopharma evaluating VBR + NrtI + Arbutus' investigational RNAi is ongoing.

†Next Generation Core Inhibitors ABI-H3733 (3733) and ABI-4334 (4334)

Expansion of Assembly Bio's Discovery & Development Efforts into New Viral Areas

Chronic Hepatitis B (HBV)

296 Million Patients[1]

High-recurrence Genital Herpes (HSV-2)

Up to 13 Million Patients[3]

Chronic Hepatitis Delta (HDV)

12 Million Patients[2]

Transplant-associated Herpesviruses (CMV, HSV-1, HSV-2, VZV)

60,000 Patients[4]

[1]WHO 2021; [2]Stockdale, J Hep 2020; [3]Gupta, et al. Lancet. 2007 (US and EU estimate of up to 13 million is based on 40% of HSV-2 symptomatic patients suffering ≥6 recurrences per year and seroprevalence; reflects upper range); [4]EBMT, OPTN, UNOS, and IRODAT (US and EU)

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- Update on 2022 Progress
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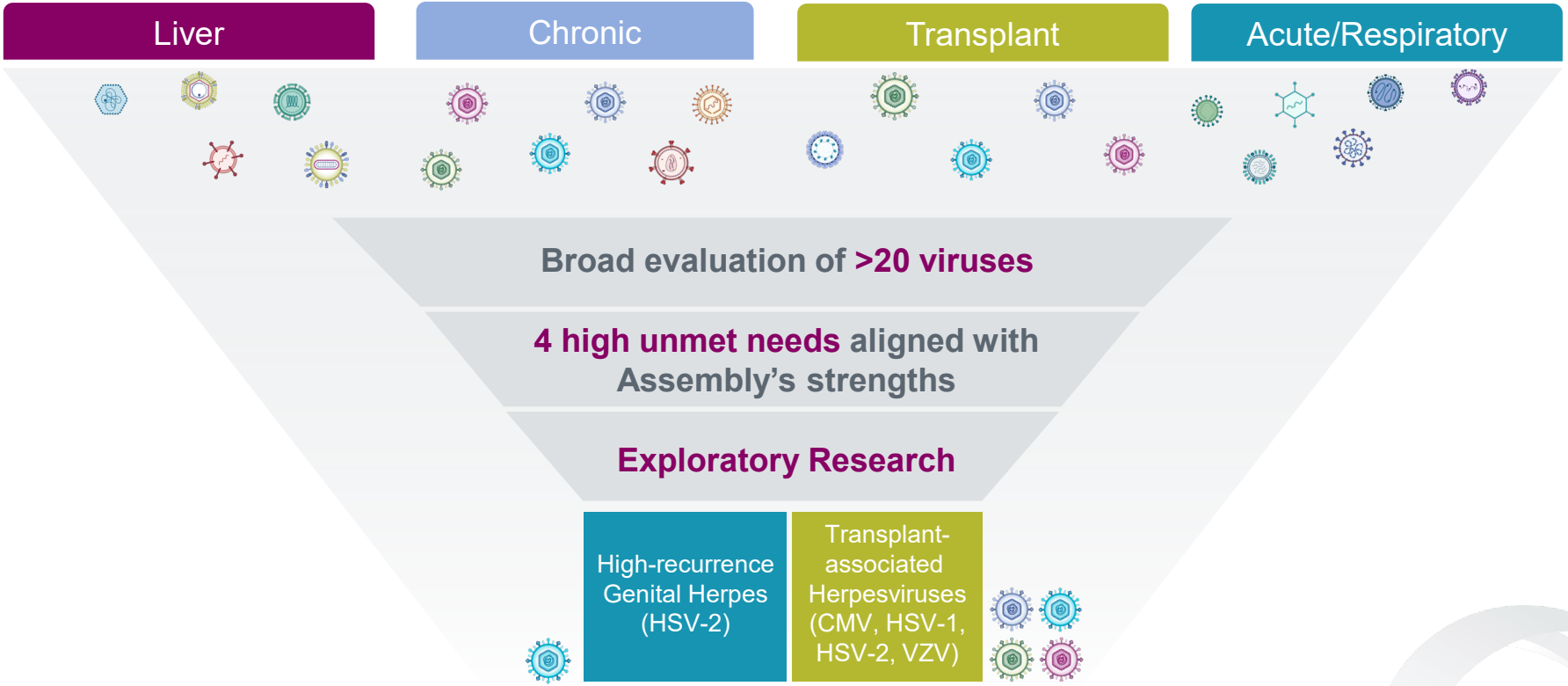
Selection of New Antiviral Opportunities for Assembly Biosciences



Expansion to New Viral Opportunities

High-recurrence Genital Herpes

HSV-2

Up to 13 Million Patients[1]

- painful recurrent lesions >6x per year
- transmission risk (including neonatal)
- increases risk of HIV infection
- psychological stress

Approved antivirals – partially effective with a high, daily pill burden

OPPORTUNITY:
a potent, long-acting injectable antiviral
to improve efficacy, adherence, and convenience

Transplant-associated Herpesviruses

CMV HSV-1 HSV-2 VZV

60,000 Patients[2]

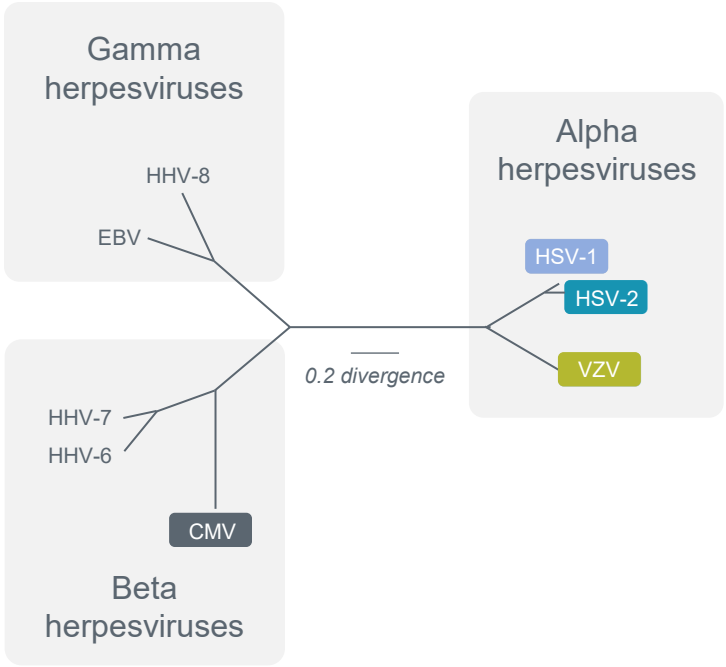
- uncontrolled viral replication and severe disease during immunosuppression
- risk of graft loss
- risk of death

Approved antivirals – narrow spectrum, with side effects and significant drug-drug interactions

OPPORTUNITY:
an oral pan-herpes antiviral to greatly simplify treatment

[1]Gupta, et al. Lancet. 2007 (US and EU estimate of up to 13 million is based on 40% of HSV-2 symptomatic patients suffering ≥6 recurrences per year and seroprevalence; reflects upper range); [2]EBMT, OPTN, UNOS, and IRODAT (estimate for transplanted-associated herpesvirus reflects US and EU only)

Herpesviruses: A Virus Family Including Several Highly Prevalent Viruses that Cause Human Disease



Herpes Simplex Virus 1 (HSV-1)

Oral herpes
Primary genital herpes
Keratitis
Encephalitis

Herpes Simplex Virus 2 (HSV-2)

Primary genital herpes
Recurrent genital herpes
Oral herpes

Varicella Zoster Virus (VZV)

Chicken pox
Shingles

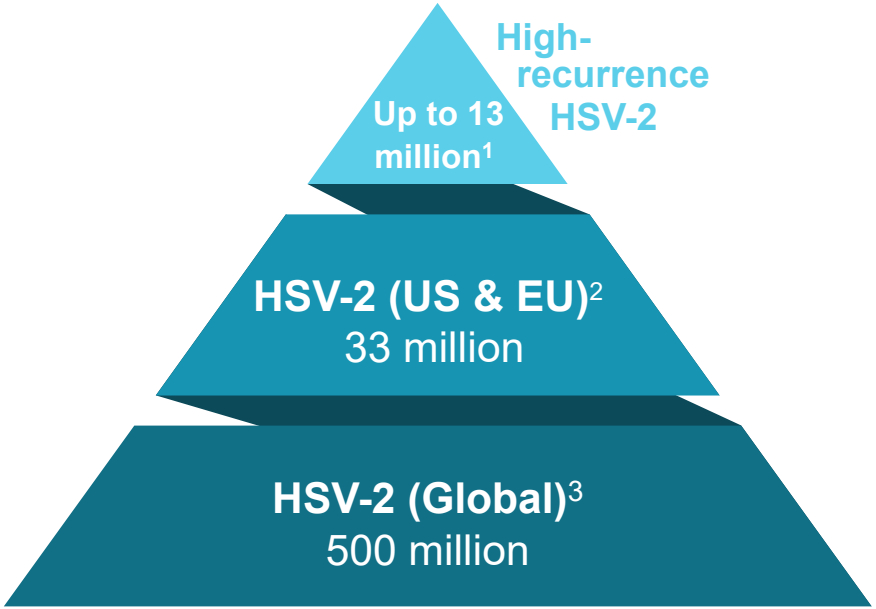
Cytomegalovirus (CMV)

Mononucleosis
Congenital CMV
Retinitis
Disseminated CMV

Borie et al. Eur. Respir. J. 2013

High-recurrence Genital Herpes

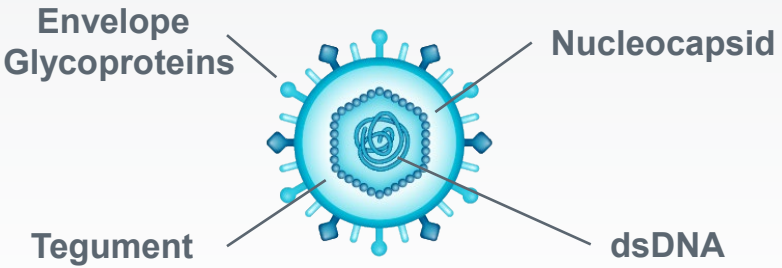
HSV-2 Epidemiology and Disease Burden



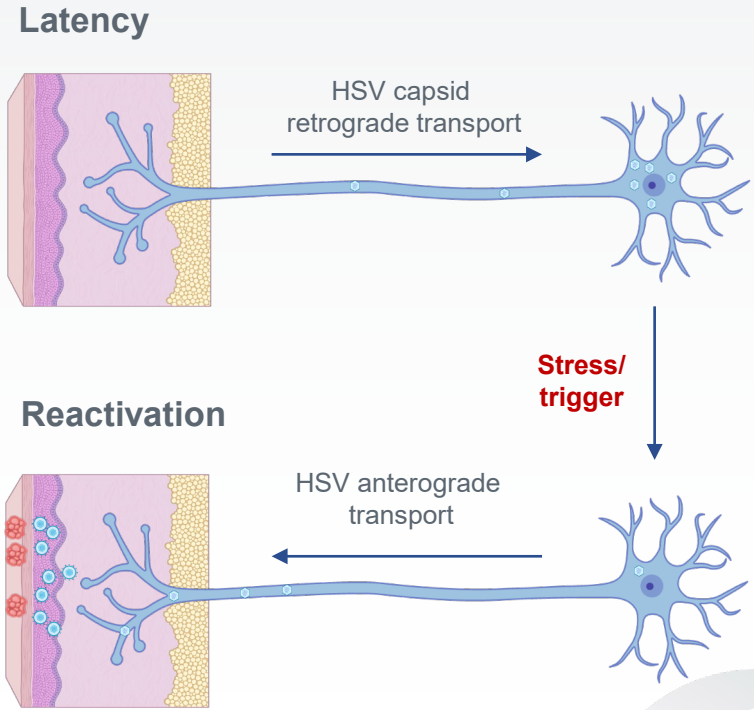
- HSV is a lifelong disease and causes painful lesions in the oral (HSV-1) and genital areas (HSV-2)
- Many HSV patients suffer frequent recurrence of lesions (≥6/year) which can be painful, severe and cause psychological stress
- HSV infection increases risk of HIV infection
- HSV can be transmitted perinatally causing severe birth defects
- Suppressive antiviral therapy is partially efficacious and requires high, daily pill burden
- Current diagnosis rates are low, and have been estimated at 10-25%[4]

[1]Gupta, et al. Lancet. 2007 (US and EU estimate of up to 13 million is based on 40% of HSV-2 symptomatic patients suffering ≥6 recurrences per year and seroprevalence; reflects upper range); [2]CDC NCHS Data Brief No. 304. 2018 (US seroprevalence data, EU estimate assumes same seroprevalence rate as US); [3]WHO Website HSV-2 seroprevalence 2016; [4]Tronstein, et al. JAMA 2007

Herpes Simplex Virus



- Large enveloped DNA virus
- Infects epithelial cells
- Maintains latency in neurons
- Reactivates during stress
- Infection is lifelong



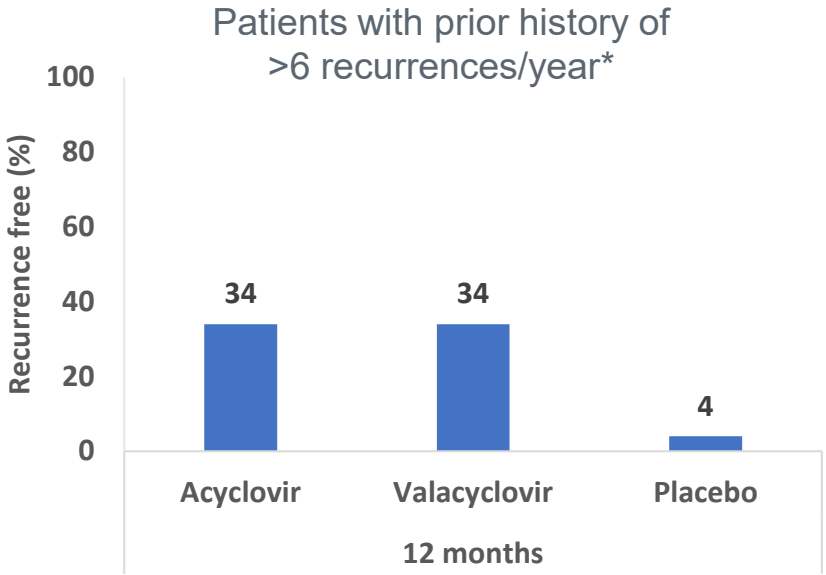
Majority of Patients with High HSV-2 Recurrence Still Experience Recurrence on Daily SOC Treatment

Suppressive regimens for patients with high HSV-2 recurrence

Acyclovir
400 mg
twice daily

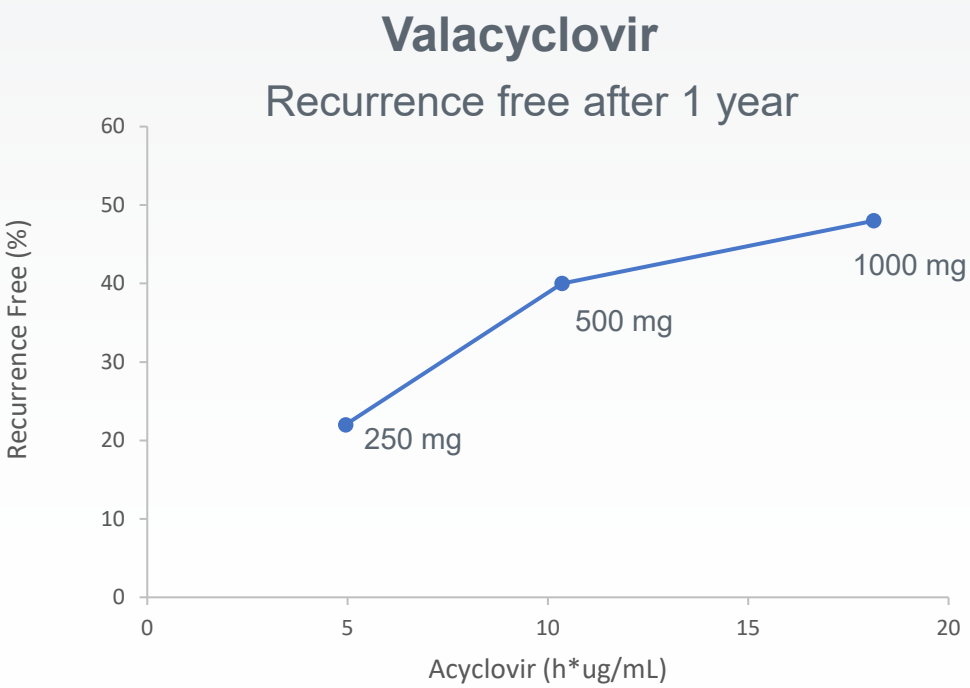
Valacyclovir
1000 mg
once daily

Famciclovir
250 mg
twice daily



*Valtrex (Valacyclovir) product insert

Improving Antiviral Exposure Reduces HSV-2 Recurrence



Chronic HSV-2 Infection – Current Unmet Need

HSV-2 causes genital herpes and frequent disease recurrence in up to 13 million patients[1]

Lowering viral load reduces recurrence frequency, viral shedding, and transmission rates

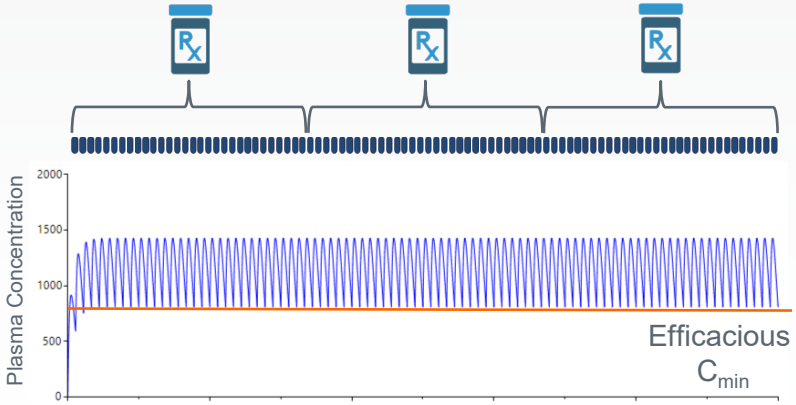
Current chronic treatment options require a high daily dose, often multiple pills/day, and are only partially effective at preventing recurrence and transmission

There is a need for more efficacious and simpler treatments for HSV patients

[1]Gupta, et al. Lancet. 2007 (US and EU estimate of up to 13 million is based on 40% of HSV-2 symptomatic patients suffering ≥6 recurrences per year and seroprevalence; reflects upper range)

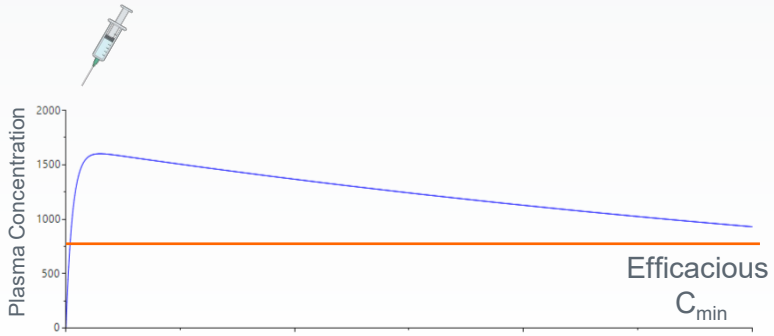
Assembly Bio's Approach: Long-Acting Injectable Antiviral Therapy

Once daily oral (90 pills)



3 months

Long-acting injectable (1 injection)



3 months

Long-acting Injectable Therapies: Rationale and Recent Advances

Benefits of Long Acting Therapies

- Ability to optimize dose, plasma concentrations
- Improved adherence

→ greater efficacy

- Eliminates mental burden, daily reminder of disease
- Greater privacy for patients, reduce stigma
- Greater convenience for patients
- Expanding treatment access

3 Approved HIV Long-acting Therapies

ViiV Healthcare

Cabotegravir, Rilpivirine

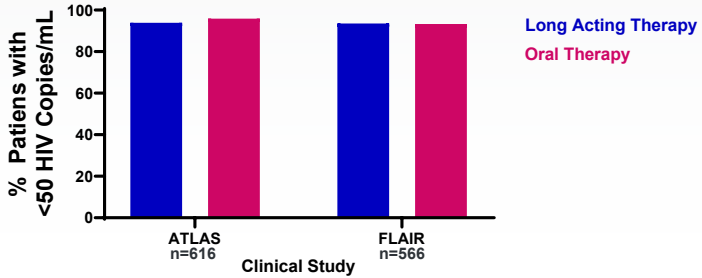
GILEAD

Lenacapavir

2 additional long-acting agents in development for HIV

Efficacy In Phase 3 HIV Studies at 48 weeks

Cabotegravir + Rilpivirine

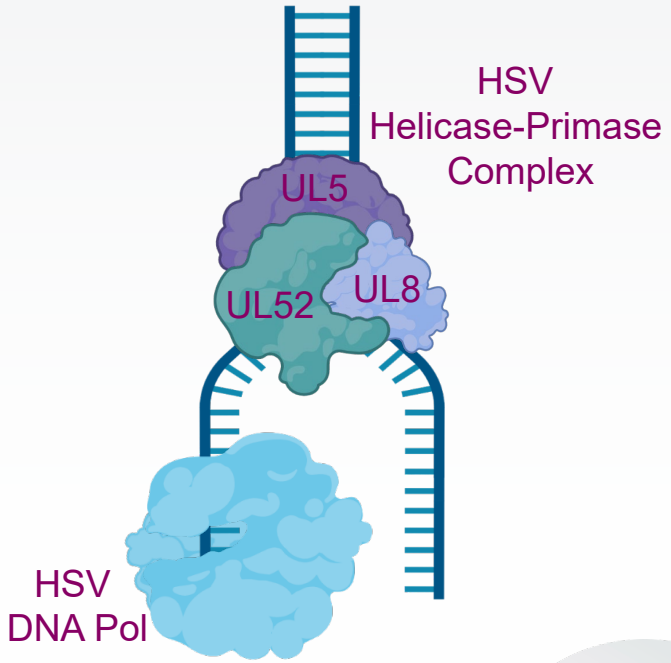


98% of responding participants from ATLAS + FLAIR HIV Studies preferred long-acting CAB + RPV over continued daily oral ART

Swindells, et al. NEJM 2020;382:1112; Orkin, et al. NEJM 2020;382:1124; Murray, et al. AIDS Behav. 2020;24:3533.

The HSV Helicase/Primase is a Clinically Validated Target

- Helicase/primase is an essential viral enzyme
- Pritelivir (phase 3 helicase/primase inhibitor) demonstrated significantly improved clinical efficacy compared to valacyclovir[1]
  - greater reductions in HSV shedding
  - fewer days with lesions
  - fewer days with pain
- Helicase inhibitors active immediately & before HSV reactivates (unlike nucleosides which require activation by viral kinase)
- Helicase/primase inhibitors are active against nucleoside analog resistant HSV
  - No clinical resistance observed with helicase primase inhibitors to date[1,2,3]



[1]Wald, et al. JAMA 2016 ; [2] Edlefsen, et al. JID 2016; ; [3] Tyring, et al. JID 2012

HSV-2 Long-Acting Inhibitor Target Product Profile (TPP)

Virologic Profile

- Potent antiviral activity against HSV-2 and HSV-1 (EC_{50} ≤ 5 nM)

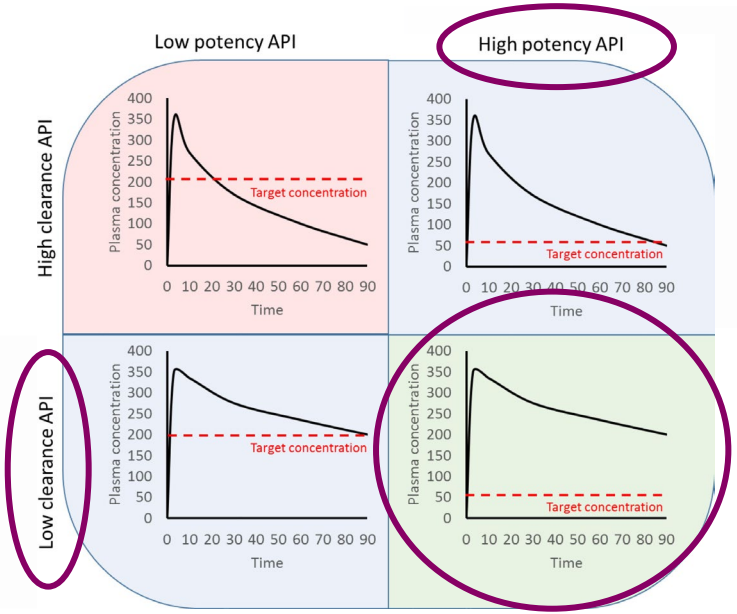
PK Profile

- Subcutaneous injection (4-6 per year)
- Plasma C_{min} ≥ 10-fold above protein adjusted antiviral EC_{50}

Safety Profile

- No clinically-significant side effects; suitable for chronic dosing
- Low potential for drug-drug interactions

Critical Properties for a Long-Acting Injectable Therapeutic



High Potency
to minimize dose that needs to be administered

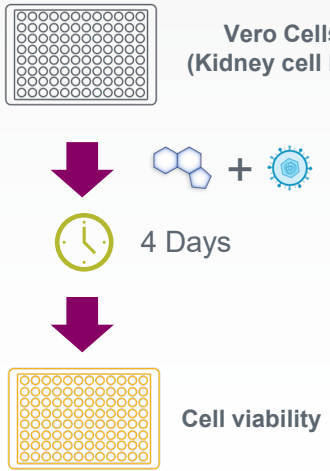
Low Clearance
to provide long $T_{½}$ and maximize exposure

- Assembly Bio's approach to incorporate ideal properties for long acting from program initiation
- Historically, drugs designed for oral absorption and can face challenges to adapt to long acting

Identification of Potent and Low Clearance Helicase/Primase Inhibitors

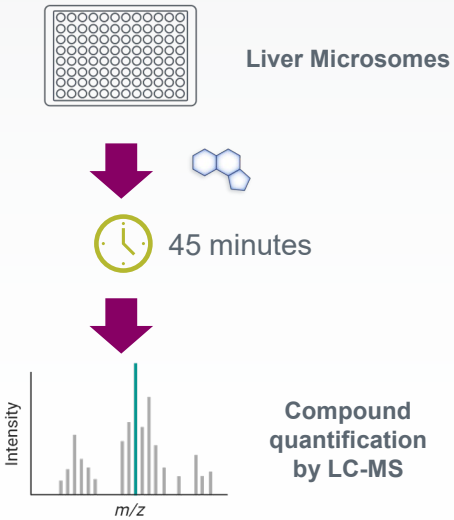
Antiviral Evaluation

HSV-1 and -2 Antiviral Assays



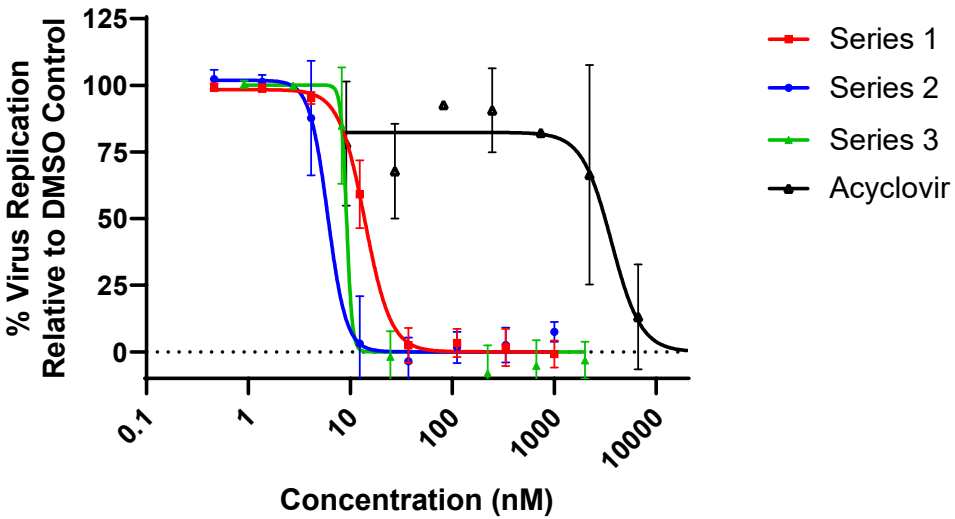
Clearance Evaluation

Microsome Stability Assay



Identification of Potent HSV-2 Inhibitors Suitable for Long-acting
Cell-based Preclinical Antiviral Activity & Microsomal Stability

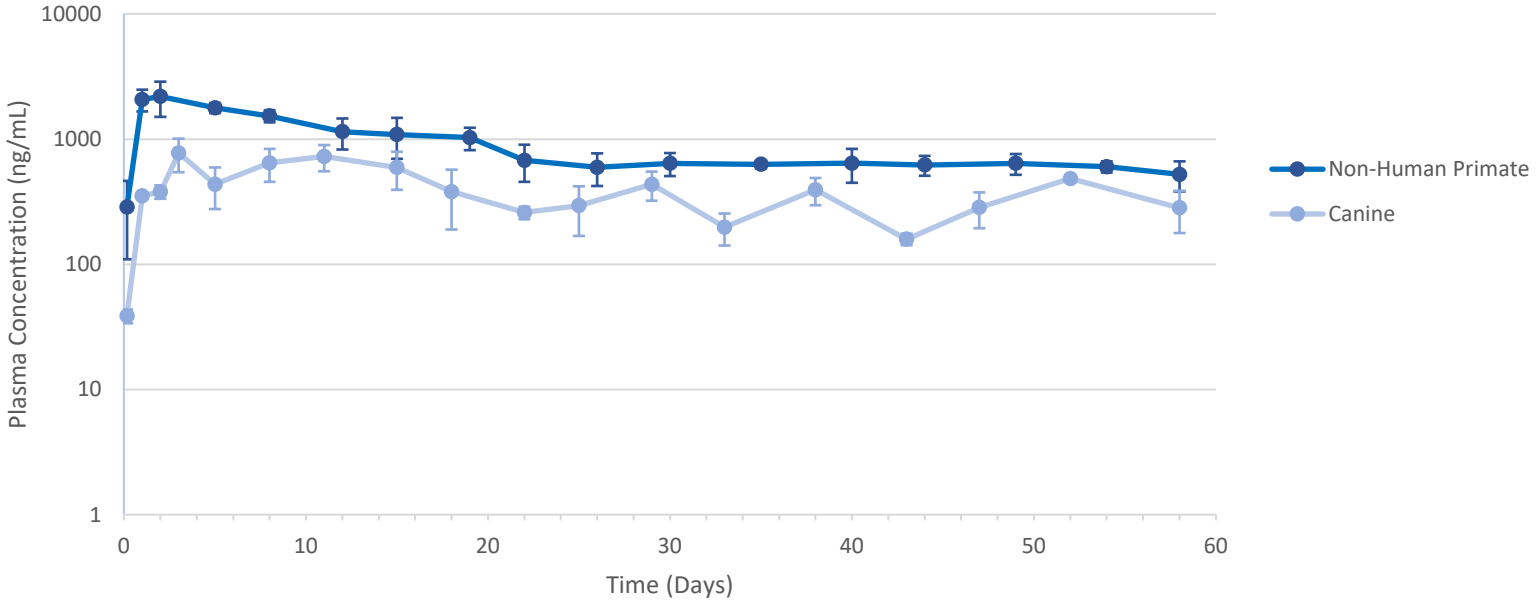
HSV-2 Antiviral Activity



Compound	Antiviral Activity EC_{50} (nM)		Human Microsomal Stability*
	HSV-1	HSV-2	
Acyclovir	3,170	3,460	NA
Series 1	13	13	96%
Series 2	9	4	77%
Series 3	12	12	96%

*% remaining after 45 min

Novel Helicase/Primase Inhibitors Demonstrate High Potential as Long-acting Agents via Subcutaneous Delivery



Single 10 mg/kg SC injection with Series 1 compound

HSV-2 Long-Acting Helicase Inhibitor: Progress and Goals

Project is progressing rapidly toward identification of development candidate

- Multiple chemically-differentiated leads with ≤20 nM potency
- Scaffolds with pharmacokinetic data that strongly support long-acting profile

- Anticipate advancing compounds into preclinical safety profiling by end 2022
- 1 of 3 preclinical programs with potential to nominate development candidate in 2023

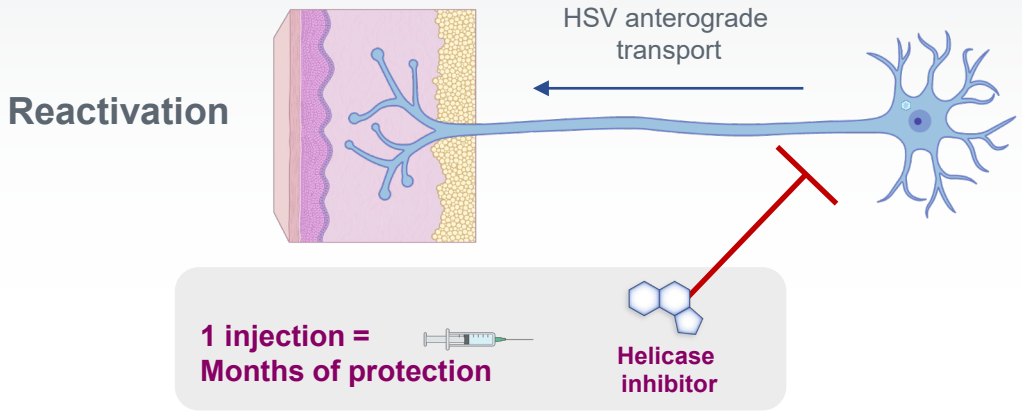
Long-Acting HSV-2 Helicase Inhibitor Project: Summary

Patients with frequent HSV-2 recurrence have a high disease burden and unmet medical need

Current therapies for HSV-2 are only partially efficacious and have high, daily pill burdens

A long-acting therapy has potential to drive greater efficacy, improve adherence and convenience

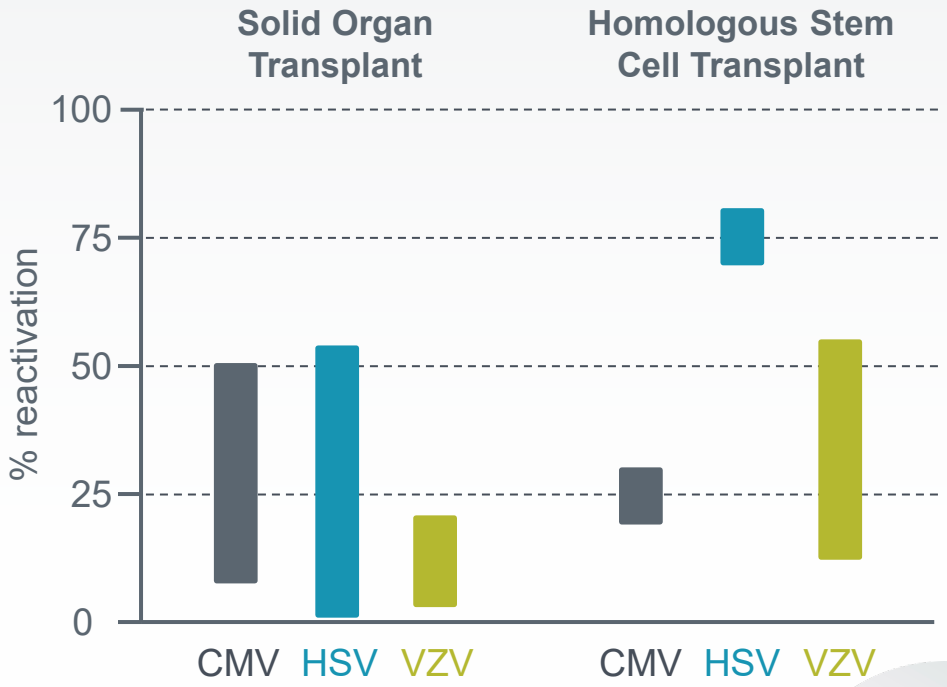
We have discovered multiple novel series of HSV helicase inhibitors with high potential as long-acting agents; we aim to progress compounds into preclinical safety testing in late 2022



Transplant-associated Herpesviruses

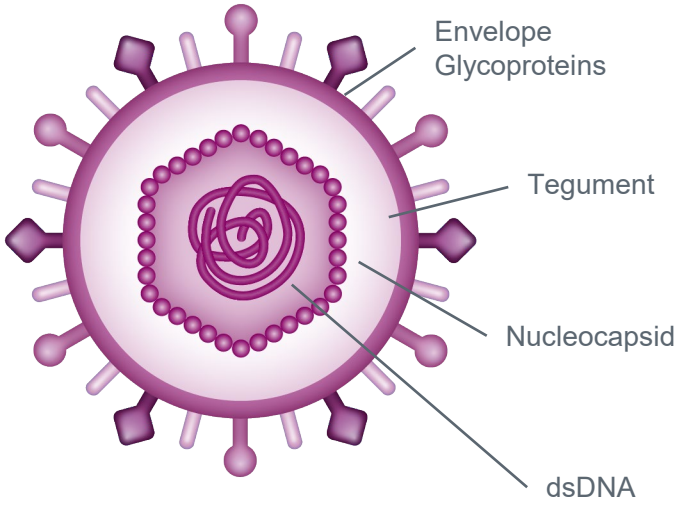
Epidemiology and Disease Burden of Herpesviruses

- Herpesviruses are highly prevalent
  - CMV positivity is ~60%
  - HSV positivity is ~60%
  - VZV positivity is ~80%
- These viruses establish lifelong latent infections and frequently reactivate in transplant patients due to immune suppression
- Viral reactivation can have severe consequences including organ rejection and death



Patel and Paya. Clin. Microbiol. Rev. 1997; Breuer, *et al.* Mol. Diagn. Ther. 2012; Clark, *et al.* Semin. Respir. Crit. Care Med. 2013; Haidar and Singh. Curr. Opin. Infect. Dis. 2019; Beyar-Katz *et al.* Clin. Microbiol. Infect. 2020; Kwon et al. Transp. Infect. Dis. 2021; Wutzler et al. Vaccine 2001; Bauer et al. BMC Infect. Dis. 2010; Reynolds et al. Public Health Rep. 2010; Lanzieri et al. Int. J. Gynaecol. Obstet. 2016; Lachmann et al. PLoS One 2018; Patton et al.Clin. Infect. Dis. 2018; Ayoub et al. BMC Med. 2019; Zuhair et al. Rev. Med. Virol. 2019; Zhang et al. Virol. J. 2022

Herpesvirus Structure

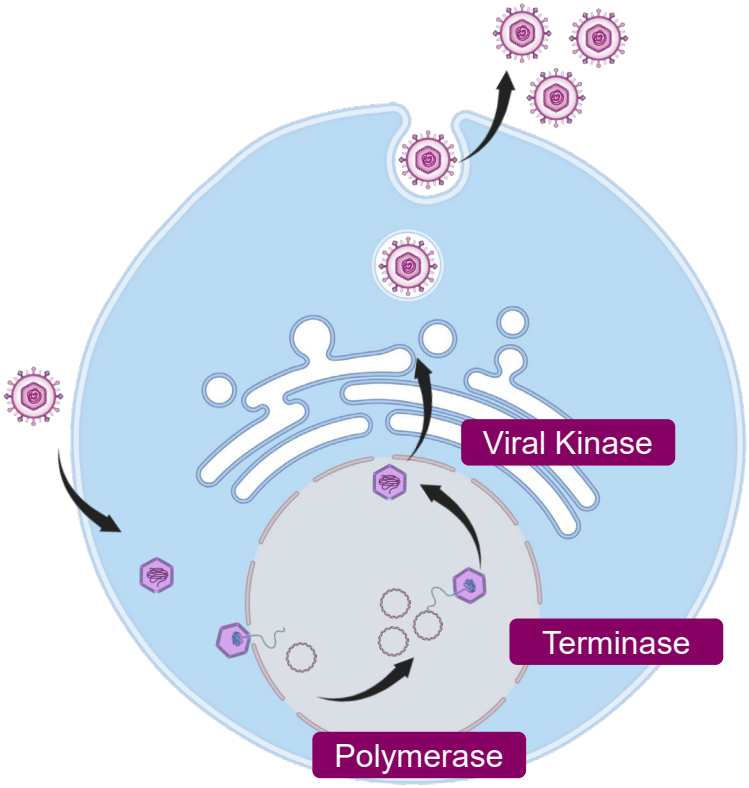


Herpesvirus		
Alpha	**Beta**	**Gamma**
HSV-1	**CMV**	EBV
HSV-2	HHV-6	KSHV
VZV	HHV-7	

- Enveloped DNA virus (~200 nm diameter, 230kb dsDNA)
- Herpesviruses encode a viral polymerase which is essential for replication
- Strong homology between herpesviruses

Herpesvirus Replication Cycle and Approved Therapies

No Single Drug Active Against All Herpesviruses



Compound	Viral Target	Approved for Use		
		CMV	HSV-1/-2	VZV
Acyclovir	Polymerase	✗	✓	✓
Famciclovir	Polymerase	✗	✓	✓
Foscarnet	Polymerase	✓	✓	✗
Ganciclovir	Polymerase	✓	✗	✗
Cidofovir	Polymerase	✓	✗	✗
Maribavir	Viral Kinase	✓	✗	✗
Letermovir	Terminase	✓	✗	✗

Rationale for a Pan-Herpes Antiviral for Immunosuppressed Patients

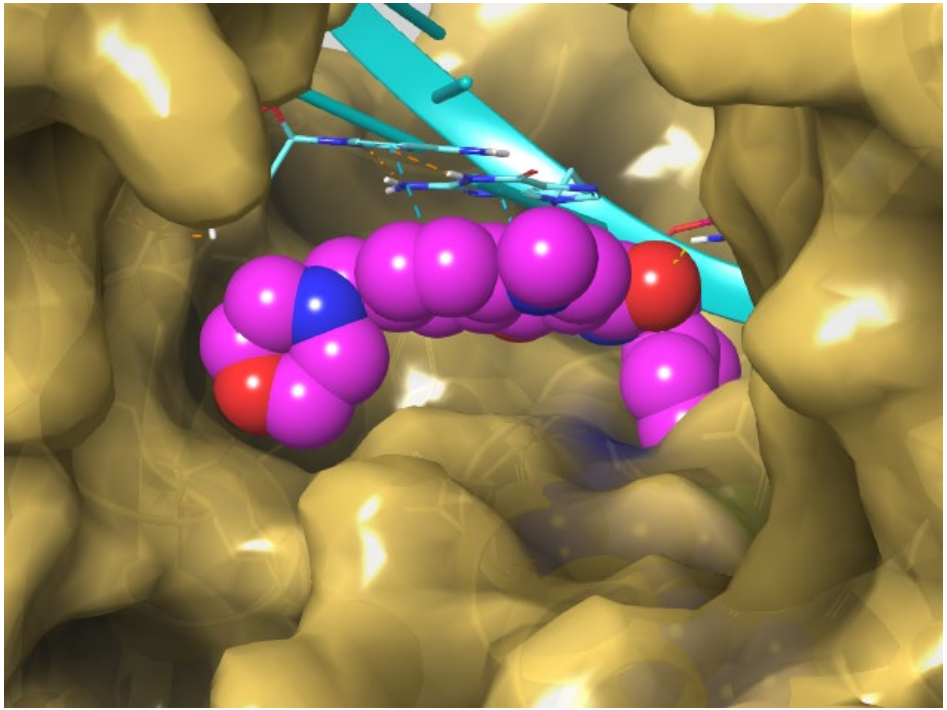
Multiple herpesviruses frequently reactivate in immunosuppressed patients and can cause severe disease

Existing antivirals do not have broad activity against clinically relevant herpesviruses

Existing antiviral therapies have further drawbacks including tolerability issues and drug-drug interactions that complicate use in immunosuppressed patients

There is need for an oral, pan-herpes antiviral that simplifies therapy for immunosuppressed patients

Assembly Bio's Approach: Develop an Oral Antiviral Active against CMV, HSV-1, HSV-2, and VZV Polymerases



- Viral DNA polymerase essential for replication of all herpesviruses
- DNA polymerases are >87% identical in active site across clinically-relevant herpesviruses
- Viral polymerase is a clinically validated target
  - early lead compounds show activity across multiple herpesviruses
- Structure-guided drug design is enabled

Pan-Herpes Polymerase Inhibitor Target Product Profile (TPP)

Virologic Profile

- Potent antiviral activity (EC_{50} ≤10 nM)
- Activity across CMV, HSV-1, HSV-2 and VZV
- Active against mutations conferring resistance to approved drugs

PK Profile

- Oral dosing (≤500 mg)
- Plasma C_{min} ≥ 10-fold above protein-adjusted antiviral EC_{50}
- Conventional formulation

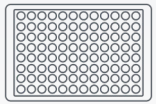
Safety Profile

- No clinically-significant side effects; suitable for long-term dosing (~12 months)
- Low potential for drug-drug interactions: critical for use in immunosuppressed patients

Establishing Antiviral Activity of Pan-Herpes Polymerase Inhibitors

Cell-based Preclinical Antiviral Assays

CMV Antiviral Assay

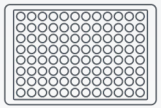


MRC-5
(Lung fibroblast
cell line)

7 Days

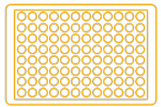
Cell viability

HSV-1 & HSV-2 Antiviral Assays



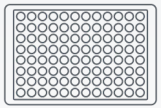
Vero Cells
(Kidney cell line)

4 Days



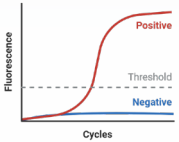
Cell viability

VZV Antiviral Assay



MRC-5
(Lung fibroblast
cell line)

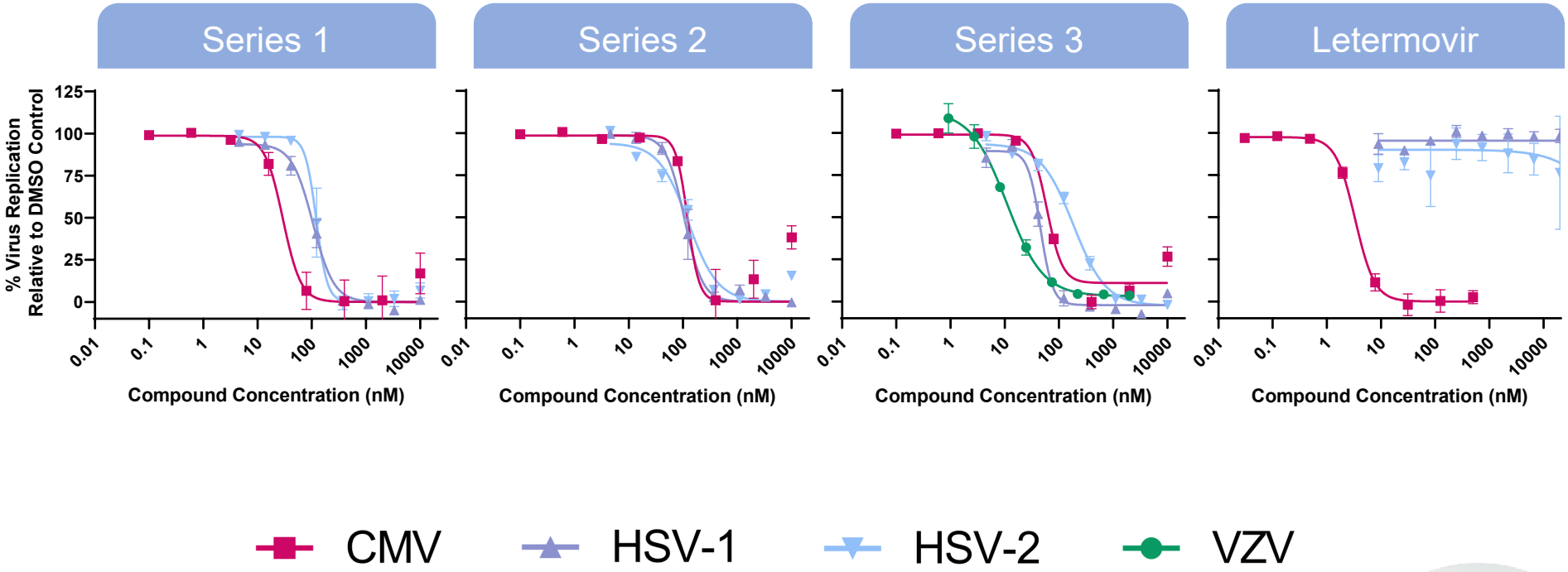
3 Days



Quantify
virus using
qPCR

Identification of Novel Potent Pan-Herpes Polymerase Inhibitors

Cell-based Preclinical Antiviral Activity



Pan-Herpes Polymerase Inhibitor: Progress and Goals

Project is in early lead optimization

- Multiple novel chemically-differentiated hits with pan-antiviral activity
- Antiviral assays developed to optimize pan-herpes activity
- Currently optimizing antiviral potency and DMPK properties

- Anticipate advancing compounds into preclinical safety profiling in the second half of 2023

Pan-Herpes Polymerase Inhibitor Project: Summary

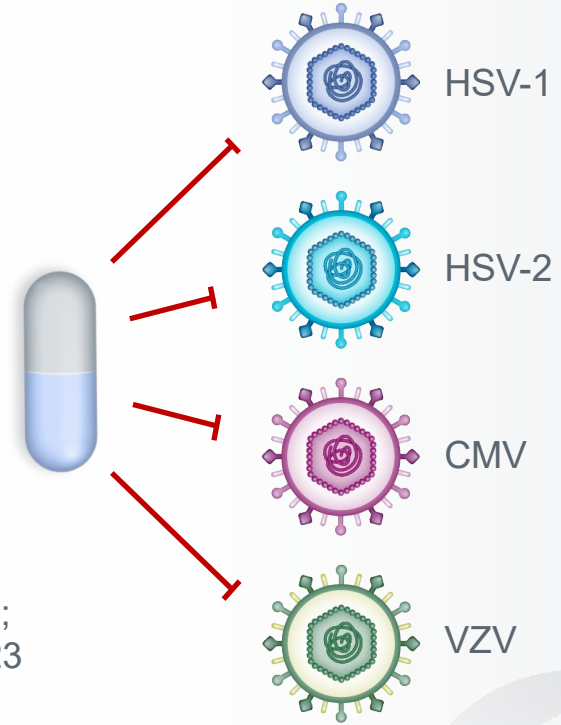
Multiple herpesviruses can cause significant morbidity and mortality in immunocompromised patients

Current antivirals are not broad spectrum and have tolerability and drug interaction limitations in immunosuppressed patients

An oral pan-herpesvirus inhibitor meeting our target profile would be a significant advance over currently used therapies

- Potential to greatly simplify treatment (one agent to control four viruses)
- Potential to improve tolerability and eliminate drug-drug interactions

3 series of potent, broad-spectrum, herpesvirus inhibitors identified; aim to advance compounds into preclinical safety testing in 2H 2023



Agenda

- Applying unparalleled expertise in virologic drug development to expand Assembly Bio's portfolio into new viral diseases
  - John McHutchison AO, MD, Chief Executive Officer at Assembly Bio
- Assembly Bio's differentiated antiviral approach for HSV-2 and an early look at the program for transplant-associated herpesvirus infections
  - William Delaney, PhD, Chief Scientific Officer at Assembly Bio
- Q&A with Sir Michael Houghton, PhD
- Update on 2022 Progress
  - John McHutchison

Sir Michael Houghton, PhD

- World-renowned scientist and Nobel laureate; international leader in virology and hepatitis
- In 1989, his laboratory and collaborators identified the hepatitis C virus and then developed blood tests that have prevented millions of infections around the world; Dr. Houghton and two others received the Nobel Prize in Physiology or Medicine for this work in 2020
- Additional areas of research include hepatitis D & B viruses, herpes viruses, noroviruses, human interferons, and SARS-CoV-1 & 2
- 40 years of experience in pharmaceutical companies including Searle, Chiron & Novartis
- Currently Director of the Li Ka Shing Applied Virology Institute and Li Ka Shing Professor in the Department of Medical Microbiology & Immunology at the University of Alberta, Edmonton, Canada
- Authored more than 300 research publications and over 70 patents
- Recipient of further international scientific prizes, including the Clinical Lasker Award (2000), the Robert Koch Medal (1993) and the Canadian CLF-CASL gold medal (2012)
- Earned his PhD in biochemistry from King's College, University of London, and was knighted in the 2021 Queen Elizabeth II Birthday Honours list for services to medicine
- Assembly Bio Board Director since July 2021

Q&A

Agenda

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Advancing a Clinical & Research Stage Portfolio of Small Molecules for HBV and Other Viral Diseases

*While Assembly Bio has discontinued further development of first-generation core inhibitor, vebicorvir (VBR), a Phase 2 triple combination study conducted in collaboration with Arbutus Biopharma evaluating VBR + NrtI + Arbutus' investigational RNAi is ongoing.

†Next Generation Core Inhibitors ABI-H3733 (3733) and ABI-4334 (4334)

Key Objectives and Anticipated Progress

2022

- ✓ Initiate Phase 1b Study – 3733
- ✓ Introduce HBV/HDV entry inhibitor program
- ✓ Introduce orally-bioavailable small molecule interferon-α receptor (IFNAR) agonist
- ✓ Introduce high-recurrence HSV-2 and transplant-associated herpesviruses programs
- ○ Initiate Phase 1a Study – 4334
- ○ Interim Phase 1b Data – 3733

2023

- ○ 3733 – Full Phase 1b Data Readout (1st Half)
- ○ 4334 – Full Phase 1a Data Readout (1st Half)
- ○ Two Development Candidate Nominations Anticipated