

June Corporate Overview

June 2019

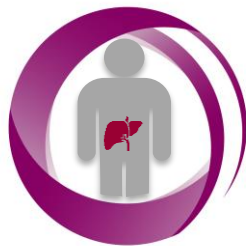
Cautionary Note Regarding Forward-Looking Statements

The information in this presentation contains estimates forward-looking statements regarding future events, including statements about the clinical and therapeutic potential of Assembly Biosciences' core protein inhibitors and Microbiome program, including ABI-H0731, ABI-H2158, ABI-H3733 and ABI-M201, the initiation, timing, progress and results of nonclinical studies and clinical studies for our HBV-cure program and Microbiome program, our regulatory strategies for our core inhibitors, economic potential of our partnered programs and the strength of our capital position. Certain forward-looking statements may be identified by reference to a future period or periods or by use of forward-looking terminology such as "designed," "expected," "likely", "may," "potential," or "projected." Such forward-looking statements, which are intended 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, are just predictions and are subject to risks and uncertainties that could cause the actual events or results to differ materially. These risks and uncertainties include, among others: outcomes of clinical studies are uncertain; the results of earlier preclinical and nonclinical studies may not be predictive of future clinical studies results; the scientific theory for our therapeutics is unproven and novel; the components, timing, patient enrollment and completion rates, cost and results of clinical trials and other development activities involving our product candidates; the duration and results of regulatory review of our product candidates by the FDA and foreign regulatory authorities; our estimates regarding our capital requirements, and our need for future capital; and the possible impairment of, or inability to obtain or protect, intellectual property rights and the costs of obtaining and protecting such rights. These and other potential risks and uncertainties that could cause actual results to differ from the results predicted are more fully detailed under the heading "Risk Factors" in our Annual Report on Form 10-K for the year ended December 31, 2018 and our Quarterly Report on Form 10-Q for the quarter ended March 31, 2019, each filed with the Securities and Exchange Commission (the "SEC") and any additional reports filed with the SEC following the date of this presentation. It is not possible for Assembly Biosciences management to predict all risks nor can it assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in any forward-looking statements. In light of these risks, uncertainties and assumptions, the forward-looking events and circumstances discussed in this presentation may not occur and actual results could differ materially and adversely from those anticipated. Any forward-looking statement speaks only as of the date on which it is made, and no obligation to update or revise any forward-looking statement is assumed, whether as a result of new information, future events or otherwise, except as required by law.



ASSEMBLY BIOSCIENCES OVERVIEW

HBV Cure



Microbiome



**Unmet Patient
Need**

No cure for almost all of the **>250 million patients** with chronic HBV

The gut microbiome is **essential** to human health, yet there are **no approved** microbiome therapies



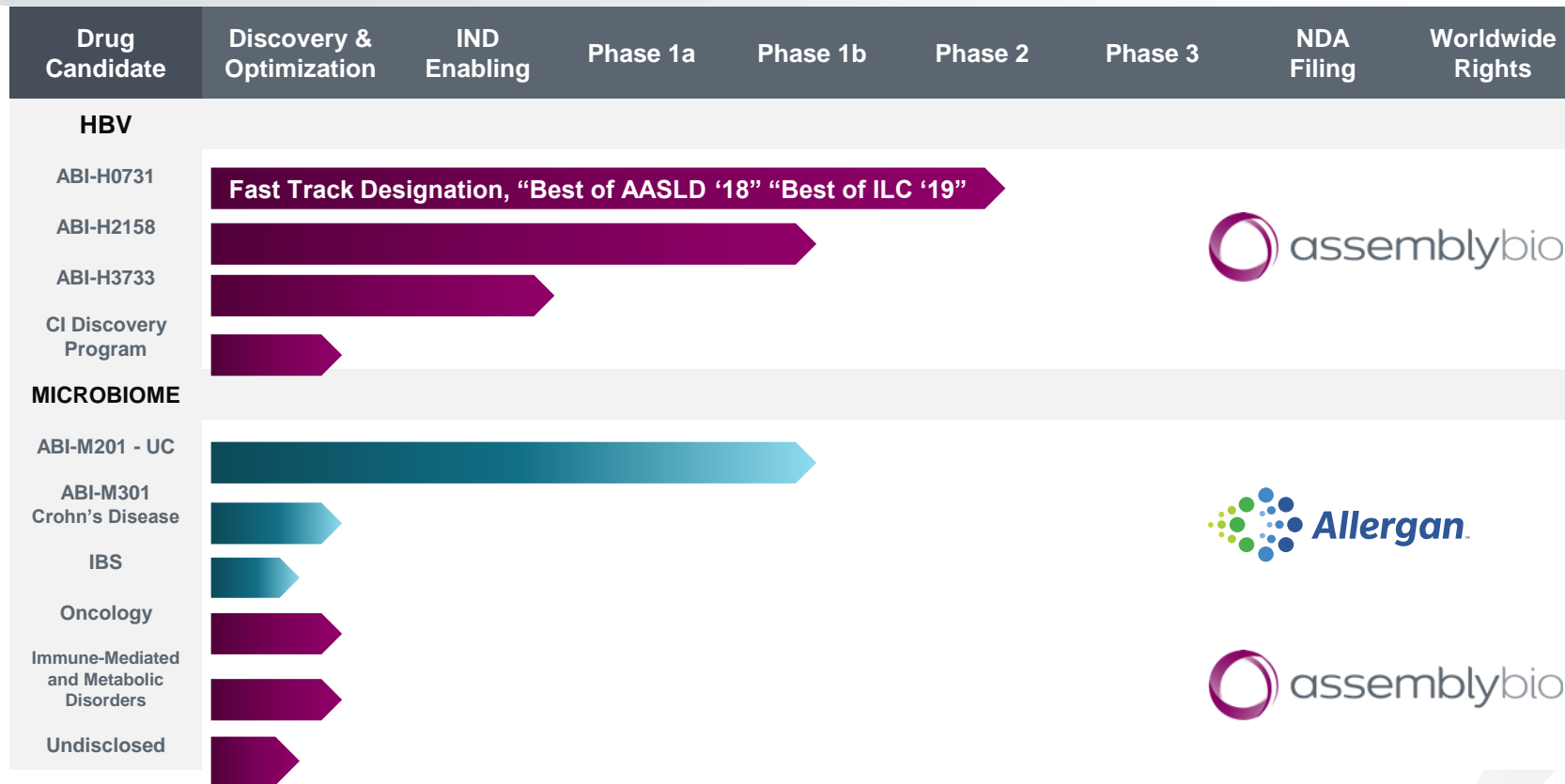
Innovation

First novel small molecule DAA in development in recent years; Designed to **break the life cycle** of HBV

First live biotherapeutic with rationally designed consortium of bacteria to be evaluated in patients with UC. Platform to address diseases far beyond gastroenterology



Development Programs Focused on Large Patient Populations with High Unmet Need

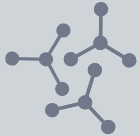


Developing a Potential Cure for Hepatitis B (HBV)

Cure is achievable

but currently at very low rates

Core Inhibitors



We believe
backbone of
curative therapy



Novel mechanism
designed to **break**
the HBV life cycle

Assembly Biosciences has a **deep pipeline of
potent core inhibitors**



What did we learn at EASL 2019?

>80% of circulating HBsAg is derived from integrated virus¹

- HBsAg may not be an appropriate biomarker of cccDNA loss
 - HBsAg does NOT lead to reinfection and is NOT a marker of ongoing infection
 - Residual HBsAg (from cccDNA) may take more time to diminish

Appropriate biomarkers of cure is an open question in the field

- If DNA and RNA are undetectable, there is likely no remaining infectious virus
- cccDNA ONLY source of pgRNA

Prolonged Nuc Therapy Fails to Eliminate Viral Replication and Low Level DNA is Infectious!

- PCR-detectable HBV DNA persists in 70-80% of patients despite TDF treatment for 5 years²
- Detected DNA represents ***infectious virus!***

EASL 2019– “Evidence for the presence of infectious virus in the serum from chronic hepatitis B patients suppressed on nucleos(t)ide therapy with detectable but not quantifiable HBV DNA”³.

- **Residual viremia refractory to elimination by Nuc therapy**
- **Likely accounts for poor cure rates**

¹Jiang, et al, EASL 2019, Poster SAT-191, ²Marcellin, et al, AASLD 2014, Poster 1861
³Burdette et al, EASL 2018, Poster PS-150



Post-EASL Key Takeaways

- ASMB is the leader in the development of core inhibitors
- Presented the first truly novel data in HBV in nearly 20 years
 - Statistically significant DNA reductions to undetectability with highly sensitive PCR
 - Statistically significant RNA reductions with patients going BLQ
- Potentially clear regulatory path for a chronic suppressive therapy superior to standard-of-care
- But the field (KOLs and investors) continues to focus on the antigens – a view that needs to be revisited



Program Designed to Assess Potential of CIs to Increase Cure Rates

Ongoing studies to define timelines for cccDNA loss, sustained suppression & potential cure



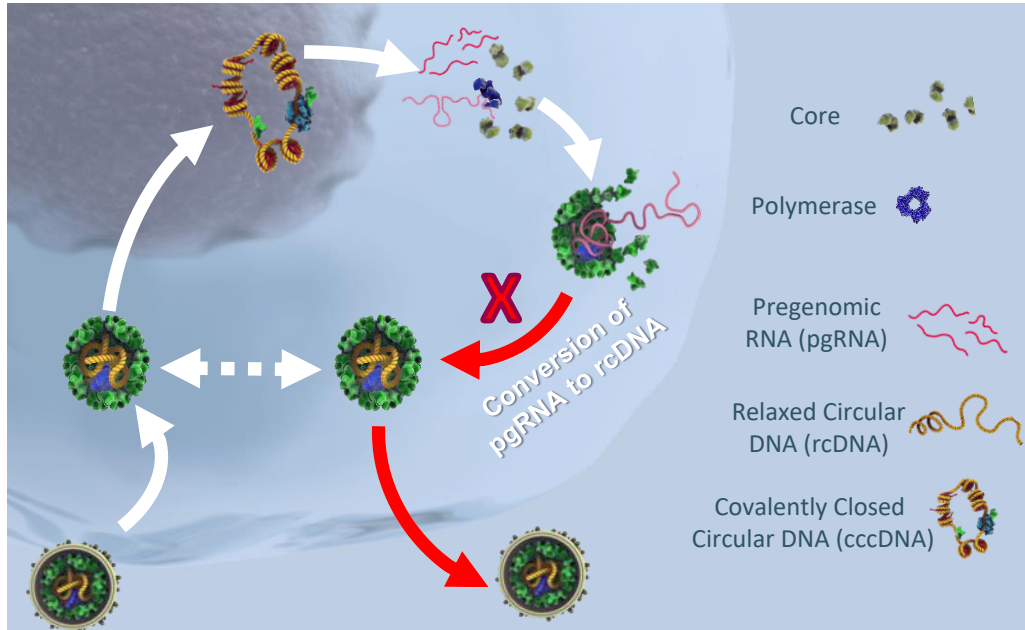
Proof of Concept for CI combination therapy is two-fold:

- 1. POC Antiviral Superiority – Elimination of viremia via DNA and RNA declines**
- 2. POC Cure –No relapse off therapy**

<https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM624695.pdf>



New Therapies are Needed to Increase Cure Rates in CHB



Nucleos(t)ide Pol Inhibitors (Nuc)

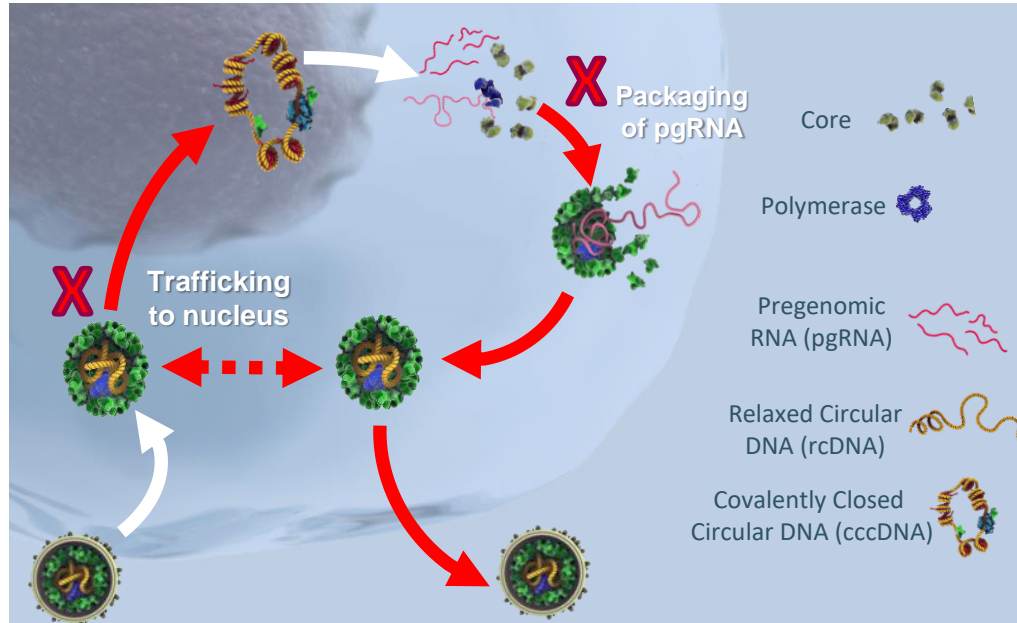
- Current “Standard of Care” for HBV
- Safe, well tolerated, with minimal resistance
- Reduce HBV DNA

But Fail to

- Eliminate virus
- Prevent new cccDNA formation
- Indefinite treatment

Cure is not possible without elimination of residual virus

CI Block Viral Replication and cccDNA Establishment



Core Protein Inhibitors (CIs)

- Inhibit multiple steps in viral replication cycle
- Achieve deeper levels of viral inhibition than Nucs alone

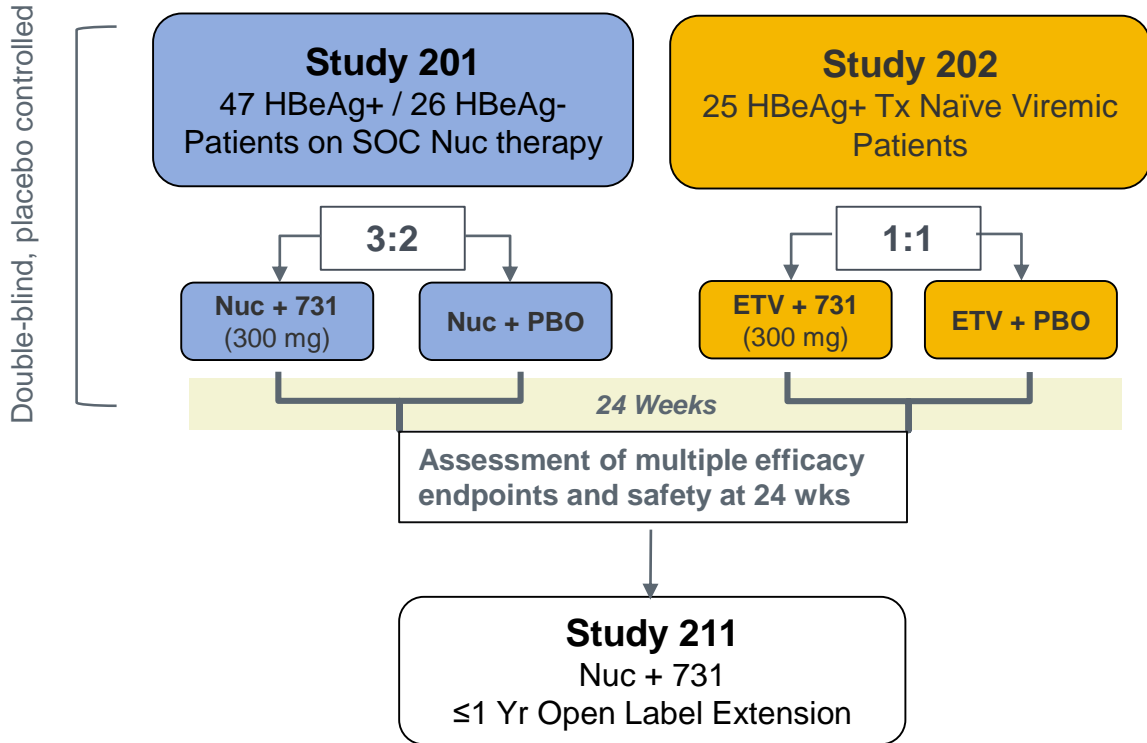
AND

- Can block the formation of cccDNA

Goal is to use combination therapy to increase cure rates with finite treatment duration

ABI-H0731: Interim Results from Ongoing Phase 2a Studies

ABI-H0731 Phase 2a Study Designs and Safety

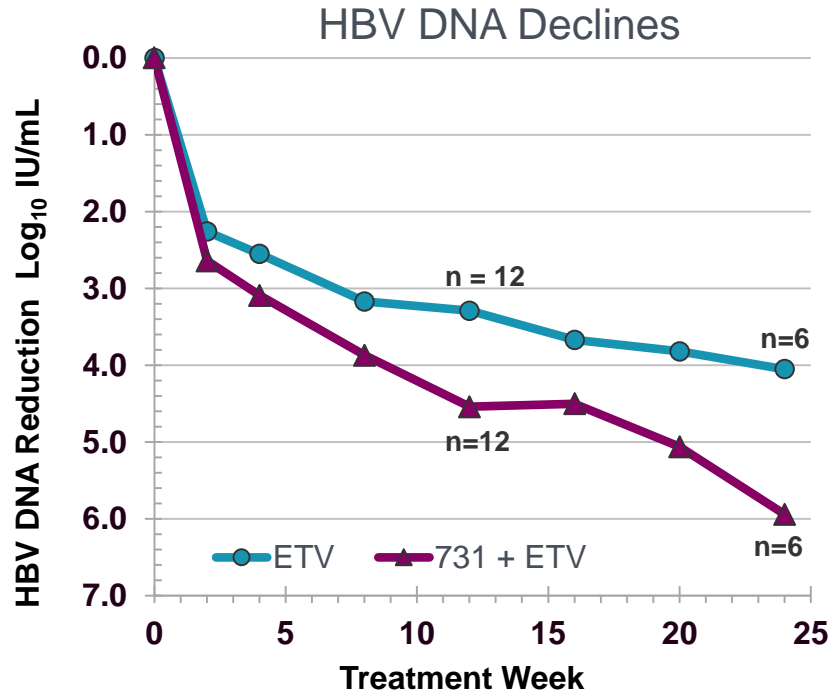


Safety

- No SAEs or treatment related discontinuations or interruptions
- Adverse events were mostly mild, infrequent, and considered unrelated to study drug
- No Flares on treatment
- No clinical AE > grade 2
- 3 patients with rash considered “possibly related” (2x grade 1, 1x grade 2); none associated with systemic findings
- Only 1 patient in each study has had a grade 2 AE considered possibly related to study drug
 - Macular/maculopapular rash—resolved on antihistamine (Study 201)
 - ALT increase—resolved with continued treatment (Study 202)



Study 202: Superior DNA Reductions with 731 Combination

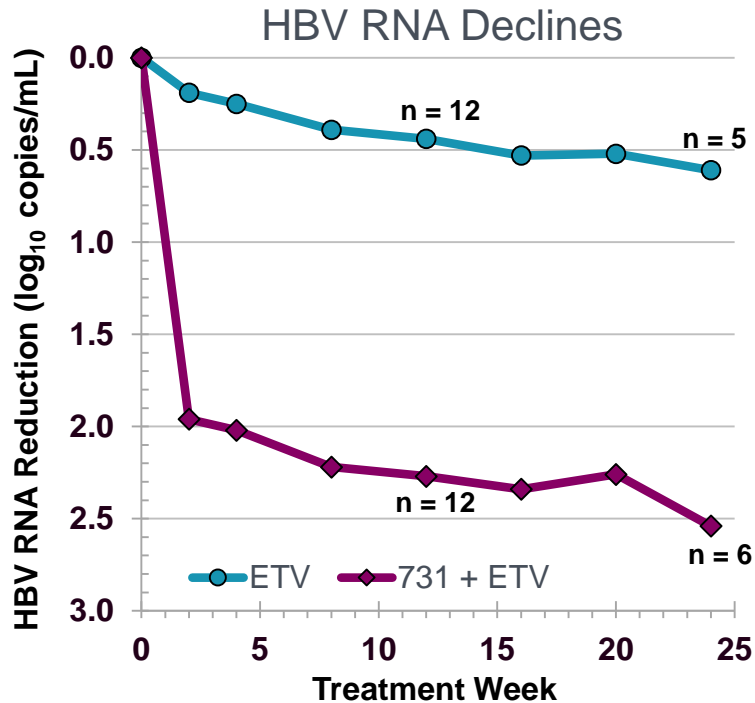


Mean Log ₁₀ HBV DNA Decline			
Week	ETV	ETV + 731	P Value
12	3.29	4.54	<.011
24	3.99	5.94	<.005

HBV DNA assessed by Roche Cobas qPCR; LOQ = 20 IU

- Significantly **faster** and **deeper** reductions in HBV DNA levels, as early as Week 2 (P=.03)
- Among subjects with abnormal ALT at entry, more rapid ALT normalization seen in combination arm
 - 5/7 vs. 0/5 by Week 4 (P <.05)
 - 7/7 vs. 2/5 by Week 12 (P <.05)

Study 202: Superior RNA Reductions with 731 Combination



Mean \log_{10} HBV RNA Decline

Week	ETV	731 + ETV	P Value
12	0.44	2.27	<.005
24	0.61	2.54	<.005

HBV RNA assessed by RT qPCR; LOQ = 200 copies/mL

- All patients on combination achieved a rapid decline in RNA levels

Elimination of Residual Viremia is an Important Unmet Medical Need

- Nucs do not eliminate HBV viremia even after years on treatment¹
- Detected DNA represents “infectious virus”
 - EASL 2019 “Evidence for the presence of infectious virus in the serum from chronic hepatitis B patients suppressed on nucleos(t)ide therapy with detectable but not quantifiable HBV DNA”²
- A highly sensitive semi-quantitative PCR assay was developed at ASMB to detect viral DNA levels to 2-5 IU/mL to monitor loss of residual virus

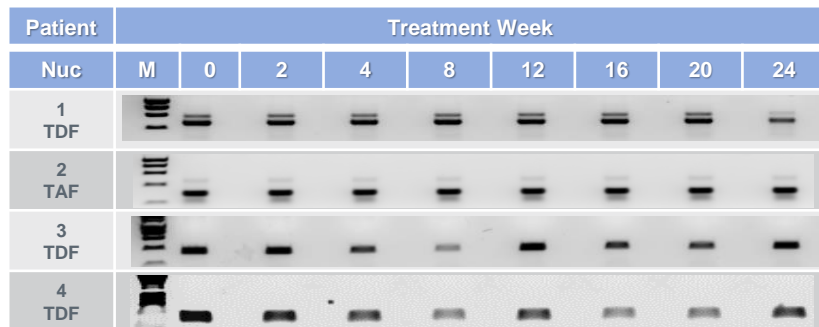


¹ Marcellin, et al, AASLD 2014, P1861, ²Burdette et al, EASL 2018, Poster PS-150

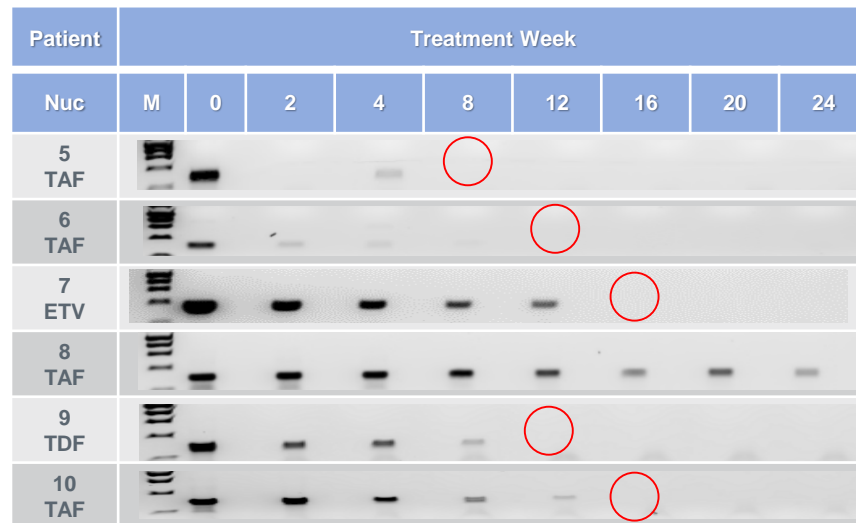
Study 201: Elimination of Detectable Virus Only on Combination

At Week 24, longitudinal serum samples were assayed for detectable virus

Nuc Monotherapy



731 Combo Therapy



HBV DNA PCR Assay To Quantitate Low Level Viremia

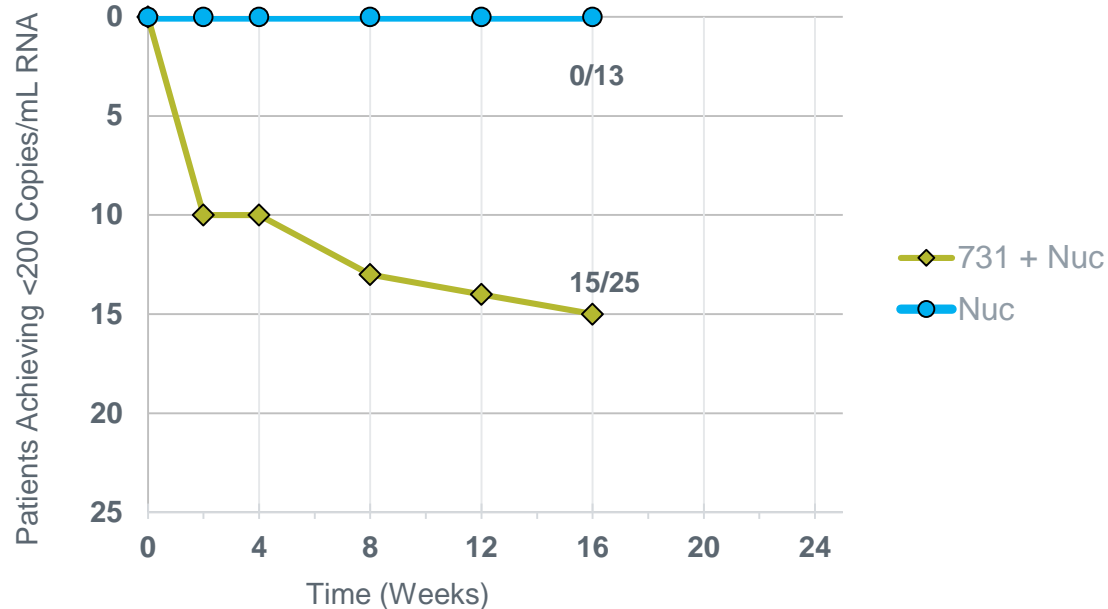
- DNA purified from longitudinal serum samples (0 – 24 Wk)
- PCR amplification (40-45 cycles) using individually optimized primers

Residual viremia is not eliminated by Nuc therapy

Elimination of detectable virus ONLY observed on combination

Study 201: RNA Reductions to BLQ Only on Combination

HBeAg Positive Patients with RNA <LOQ at Baseline (N = 38)



- All subjects on combination arm achieved rapid RNA declines



Study 201: Antigen Declines at Interim Analysis

Patients Treated 24 Weeks*		
Treatment	Nuc	731 + Nuc
DNA (TND ¹)	0/4 (0%)	5/6 (83%)
RNA (<200 Copies/mL)	0/3 (0%) ²	3/6 (50%)
HBeAg \geq 0.5 Log ₁₀ Decline	0/3 (0%)	1/6 (17%)
HBsAg \geq 0.5 Log ₁₀ Decline	0/4 (0%)	0/6 (0%)

¹ Target not detected by ASMB semi-quantitative PCR

² a 4th subject on Nuc was BLQ at baseline

*Subjects with available data

- Antigen declines may not be accurate early biomarkers for cccDNA loss
- Study subjects continue to be treated and followed in open label Study 211
- Safety, viremia and viral antigens continue to be monitored over time



Summary of Interim Data for Phase 2a Studies on ABI-H0731

Favorable safety and tolerability profile

- AEs and lab abnormalities were generally considered unrelated, grade 1 and transient

Combination of 731+Nuc demonstrated superior antiviral activity vs. Nuc alone

- In treatment naïve patients, faster and deeper declines in HBV DNA observed starting at Week 2
- In Nuc “suppressed” patients, HBV DNA reductions to below limits of high-sensitivity PCR assay
- In both studies, significant HBV RNA declines

Elimination of residual viremia will likely be required to prevent new cccDNA formation and increase cure rates

Ongoing Studies to Define Timelines to cccDNA Loss, Sustained Suppression & Potential Cure



ABI-H2158: Second Generation Core Protein Inhibitor

Phase 1a Safety, Tolerability and PK in 48 Healthy Volunteers

- No dose dependent TEAEs, pattern of clinical safety or laboratory abnormalities observed
- Exposures increased in a roughly dose-proportional fashion
- Steady-state concentrations achieved quickly in the MAD cohort, with accumulation of ≈ 1.5 -fold at steady state
- No significant food effect observed

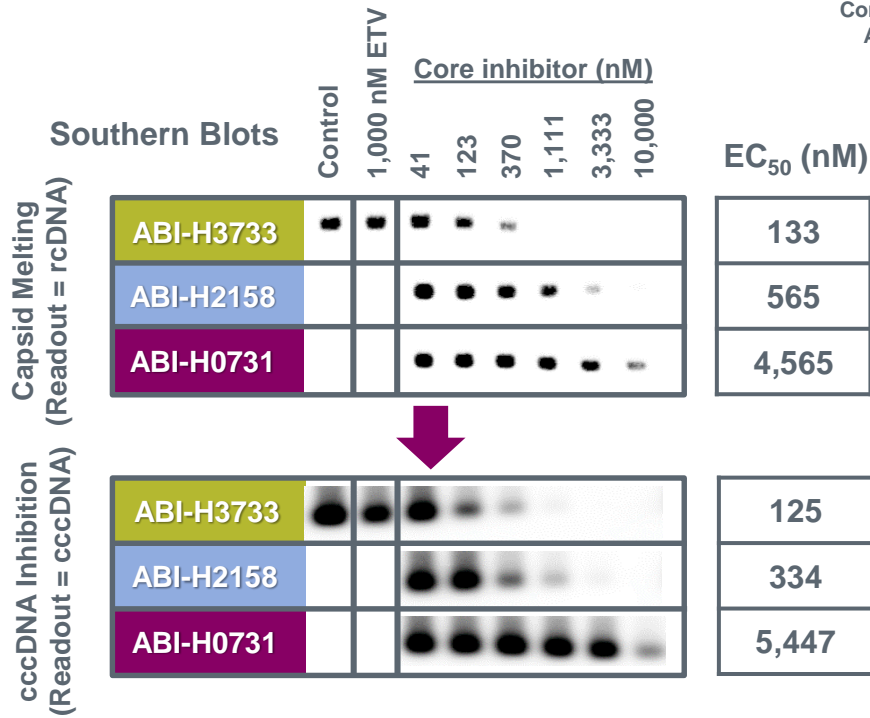
Trough liver concentrations are projected to exceed the *in vitro* EC₉₀ (334 nM) for inhibition of cccDNA establishment with QD dosing of 100 mg and higher

Phase 1b ongoing...

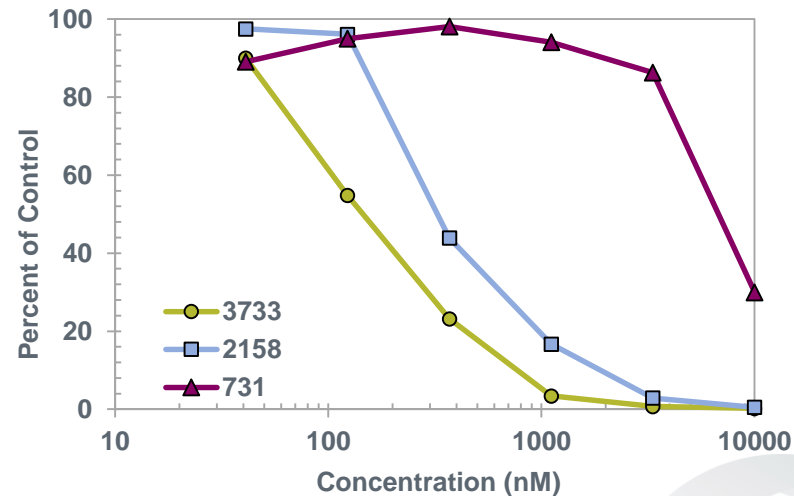


ABI-H3733: Relative Potency in Blocking cccDNA Generation

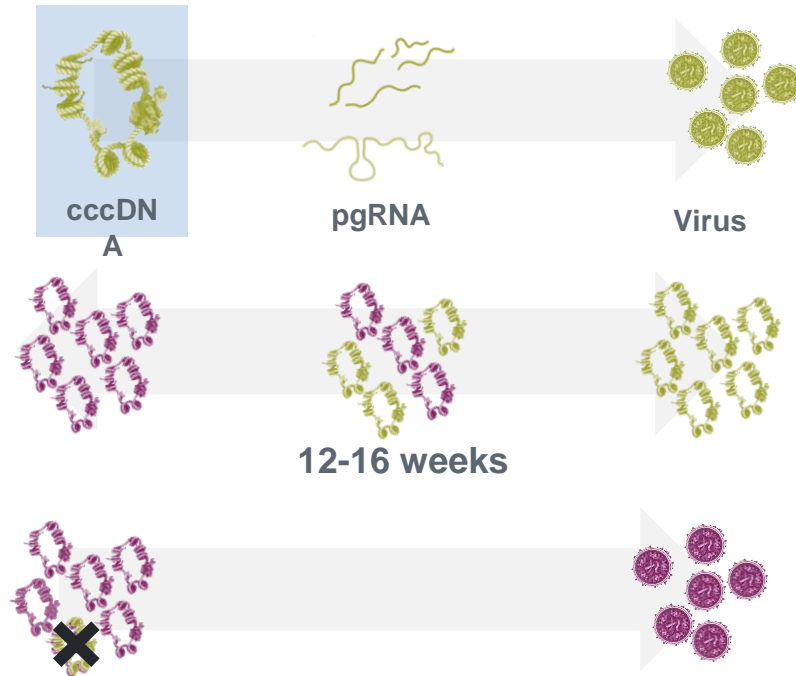
HBV Infection of HepG2-NTCP Cells



Inhibition of cccDNA Establishment



Summary Results From Expanded cccDNA Biosynthesis Study



- Genetic source of resistance shown to be cccDNA
- pgRNA closely reflects genetic composition of cccDNA pools
- Turnover of cccDNA from sensitive to resistant and from resistant to sensitive occurs in 12-16 weeks
- Suggests relatively rapid biologic turnover of both pgRNA and cccDNA pools and/or infected cells
- No evidence to support existence of inactive subpopulation of cccDNA, as genetic changes are observed in the entire population of cccDNA

Results indicate that existing cccDNA has a limited half-life, suggesting that therapies inhibiting establishment of new cccDNA may lead to higher cure rates for patients with HBV

Highlights and Next Steps

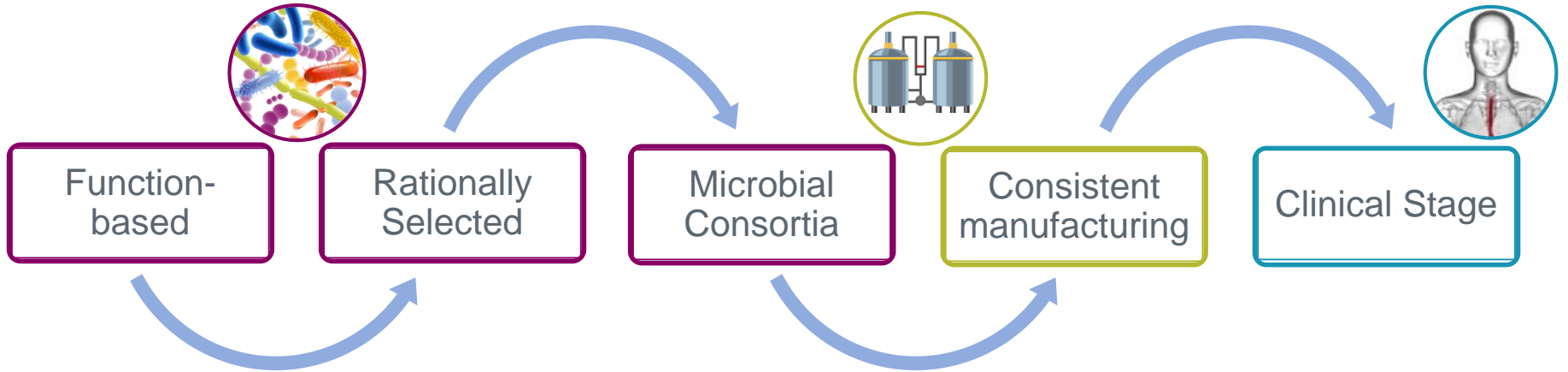
- **Nucs are effective, but do not eliminate residual HBV DNA and HBV RNA**
- **Combination of 731+ Nuc demonstrated potential to eliminate residual HBV DNA**
- **Core Inhibitors have the potential to be the backbone of future HBV regimens**
 - We believe that elimination of residual viremia will likely be a critical milestone required to increase rates of cure
- **2158 currently in dose finding Phase 1b study and Phase 2a studies expected to follow immediately**
- **3733 expected to initiate Phase 1a study in early 2020**
- **Initiating discussions with global regulatory bodies regarding design of next studies and pathways to approval for 731 + Nuc combination**



Microbial Biotherapeutics

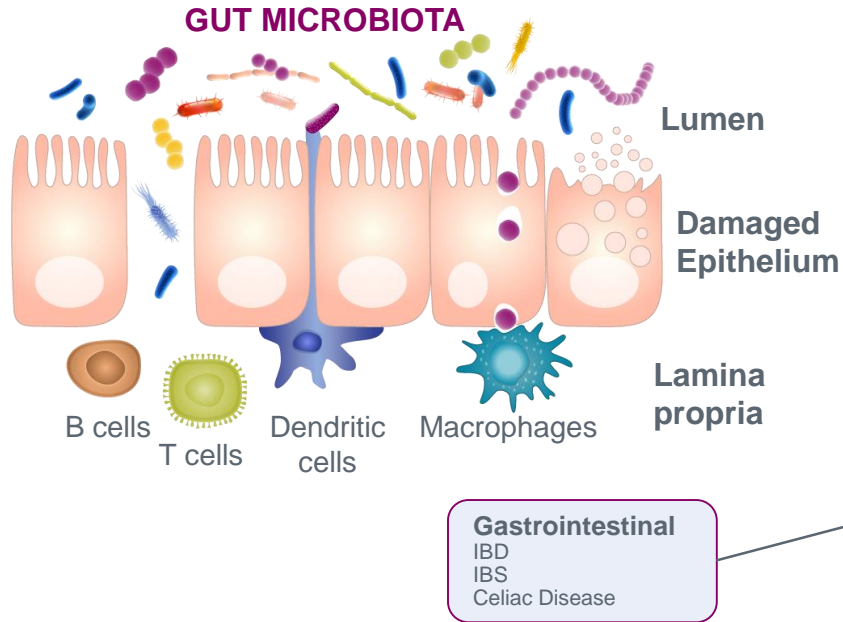
Harnessing the therapeutic potential of the human microbiome

Developing Best-in-Class Microbial Biotherapeutics

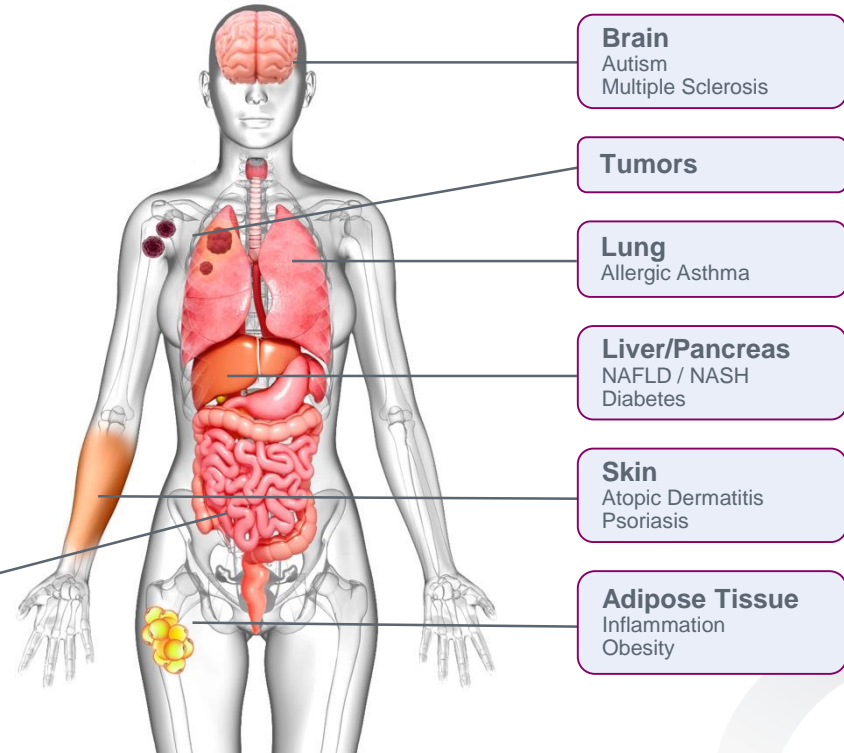


Gut Microbiota Drives Multiple Disease Consequences

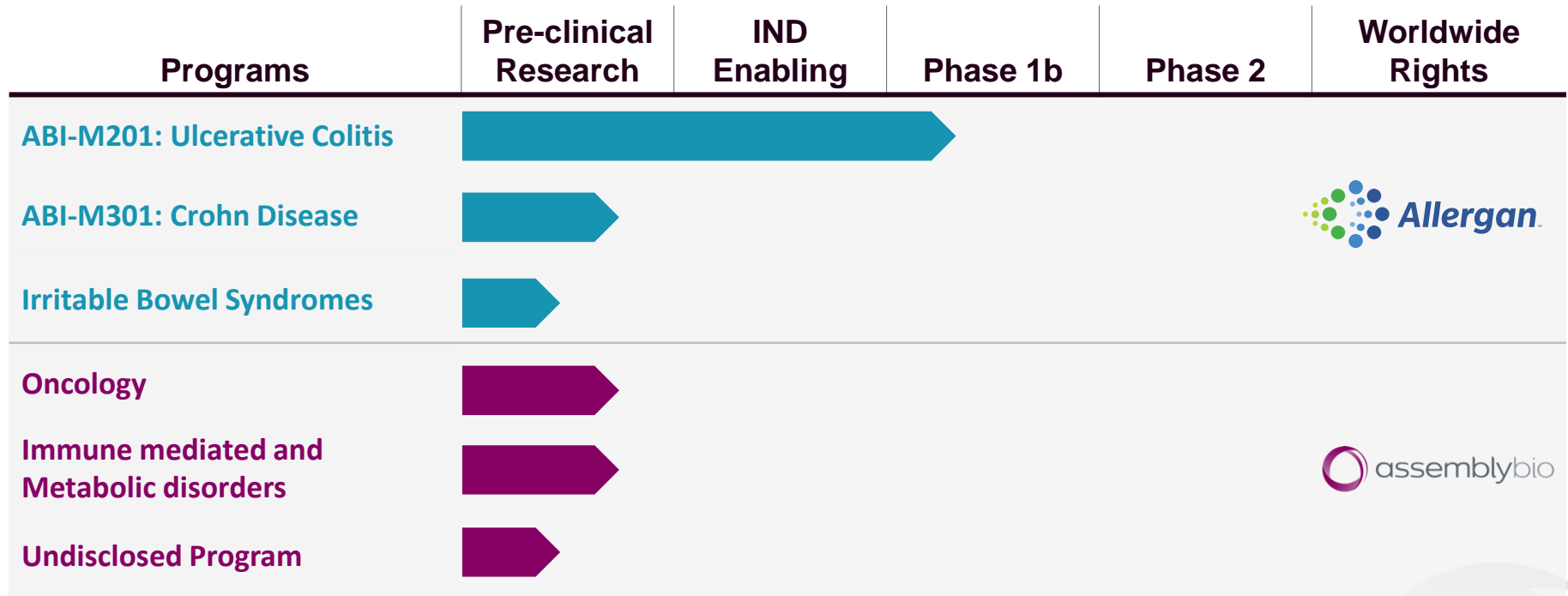
Local disease consequences



Systemic disease consequences



Broad Biotherapeutic Pipeline



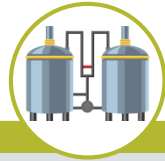
Concept-to-Clinic R&D Platform

Integrated therapeutic discovery and development capabilities



Rationally Selected Bacterial Consortia

- Commensal bacterial library isolated from healthy human donors
- Rigorous human cell-based assays with MOA's relevant to disease
- Microbial phenotyping & genomic analysis support, selection & IND filing
- *In vivo* biologic models to evaluate live microbes in context of relevant biology



Differentiated Manufacturing

- Optimized growth methodologies for anaerobic bacteria
- Lyophilized formulation development
- Process scalability and high quality GMP production
- Manufacturing capabilities for in-house drug product



Gemicel® Targeted Oral Delivery Technology

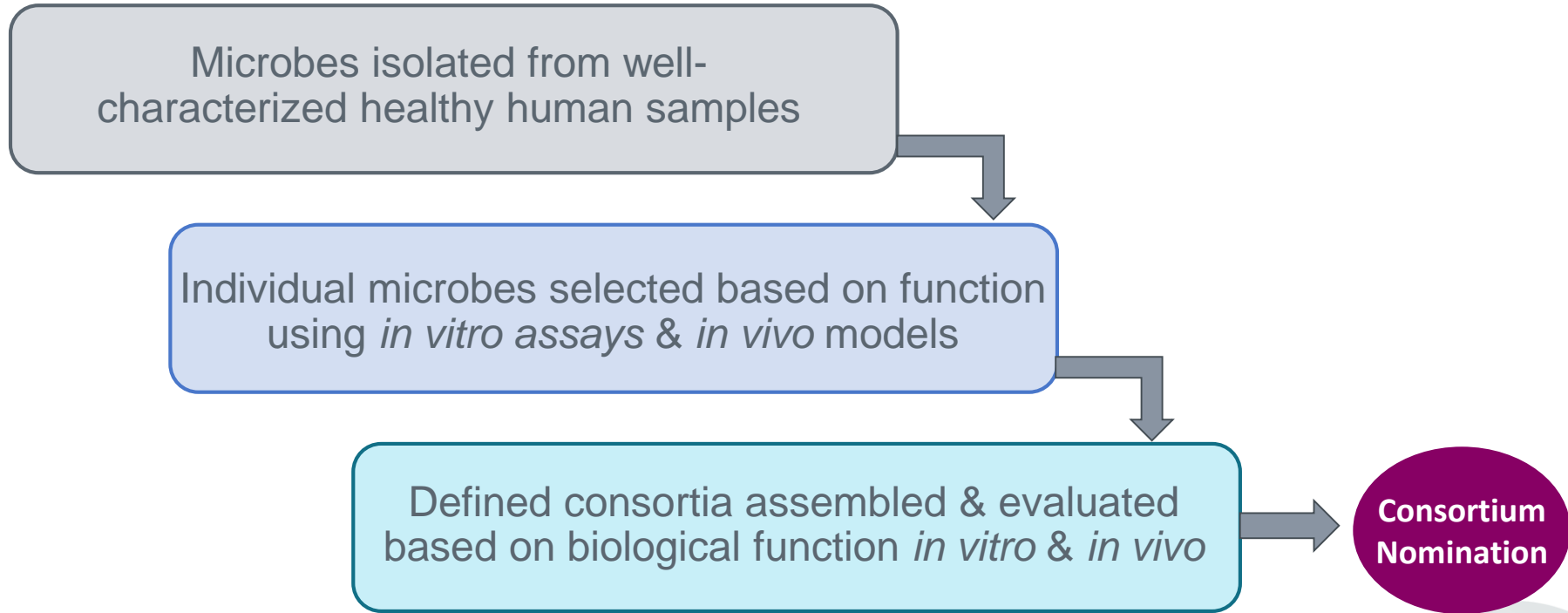
- Novel dual release technology
- Deliver vegetative bacteria to specific intestinal regions
- Two different doses of same drug or two different drugs



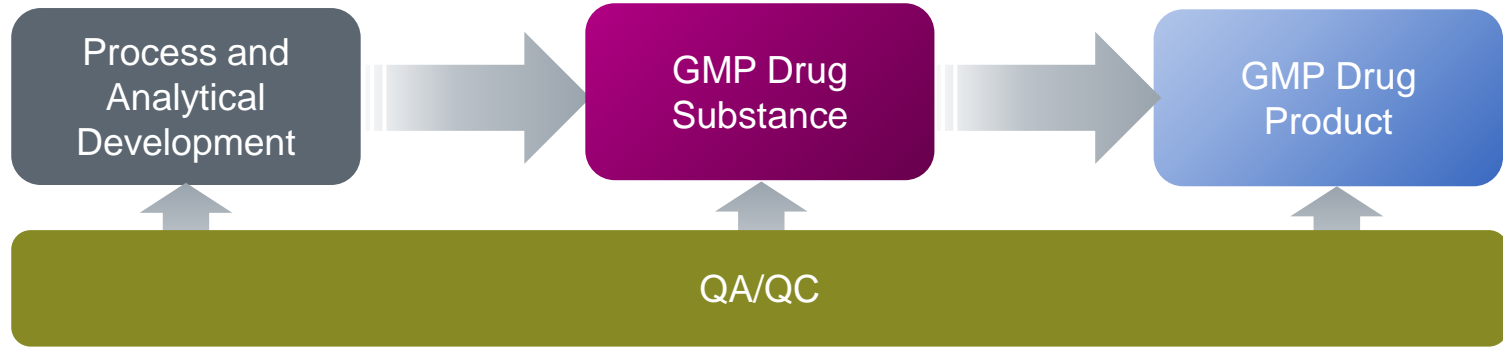
Clinical Development

- Ph1b in progress for M201 in patients with UC

Rationally Selecting Consortia of Live Microbes with Pharmacological and Biological Functions



Scalable GMP Drug Manufacturing Processes and Encapsulation



Fully integrated CMC capabilities for live microbial biotherapeutics

Maintain microbial viability and biological function

Reproducible process batch to batch using proven technology

Taxa from any bacterial phyla are candidates for use



Gemcel® Capsule-In-Capsule Delivery Technology



Oral delivery of viable vegetative bacteria with dual release



Gemcel® capsule



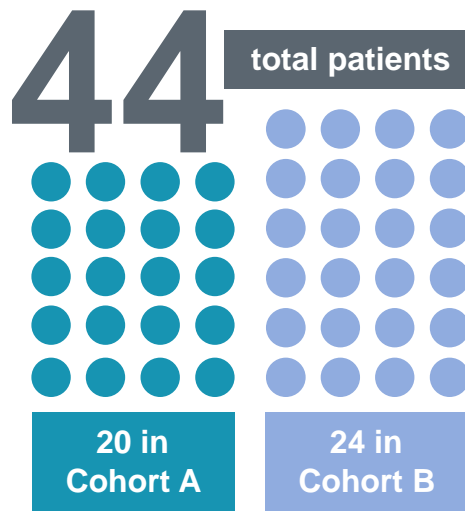
Dual, bolus release to multiple regions of the gastrointestinal tract

API = active pharmaceutical ingredient.



About the study

- ✓ Phase 1b
- ✓ Randomized
- ✓ Double-blind
- ✓ Placebo-controlled
- ✓ Patients with mild-moderate UC



8-week treatment with QD orally administered ABI-M201 or placebo

8-week clinical endpoints

Safety and tolerability

Induction of clinical remission

Endoscopic improvement

Gastrointestinal Collaboration with Allergan



- Responsible for discovery and development through proof of concept (POC)
 - Ulcerative Colitis
 - Crohn's disease
 - Irritable Bowel Syndromes
- ABI-M201 Phase 1b in patients with mild-to-moderate UC underway




- Develops programs post-POC
- Reimburses ASMB two-thirds of R&D cost up to \$75 million collectively

Financial Highlights

- **\$50 million up-front** payment
- **\$75 million in R&D** funding
- Up to **~\$2.8 billion in development** and commercial milestones
- Tiered royalties up to midteens

Key Achievements of Microbiome Program

 **Partnership with Allergan** in IBD & IBS – up to \$2.8 billion in milestone payments

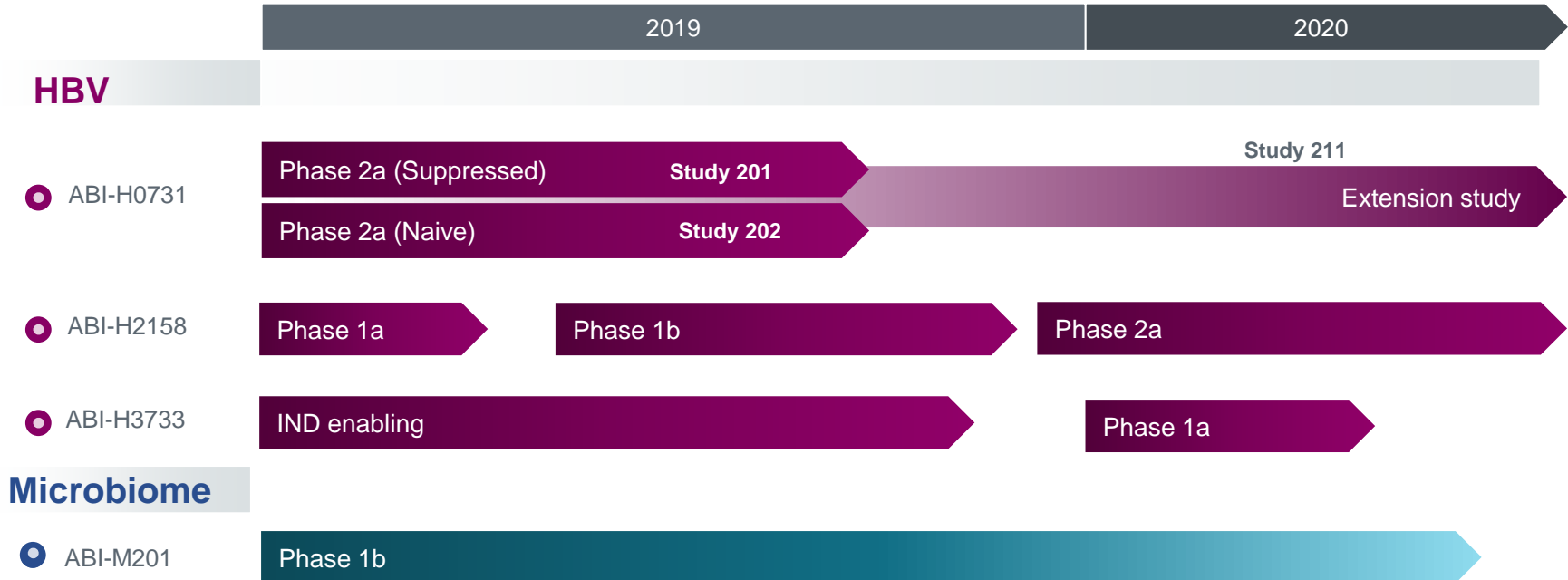
 **Phase 1b clinical trial underway** for ABI-M201 in patients with ulcerative colitis

 **M201 discovery to IND in less than 12 months** – Established R&D roadmap

 **6 pipeline programs** in high value Indications

 **High quality, scalable manufacturing** facility and processes established

Strong Trajectory in 2019: Upcoming Milestones



STRONG BALANCE SHEET: ~\$193M in cash (as of 3/31/2019)

