



Inarigivir ACHIEVE Trial Results and HBV Clinical Program Update

August 2, 2018



FORWARD LOOKING STATEMENT

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our product candidates; whether certain top-line results from our clinical trials materially change as more information becomes available; whether results obtained in preclinical studies and clinical trials will be indicative of results obtained in future clinical trials; whether inarigivir, SB 11285 and any of our other product candidates will advance through the clinical trial process on a timely basis and receive approval from the United States Food and Drug Administration or equivalent foreign regulatory agencies; and whether, if inarigivir, SB 11285 or any of our other product candidates obtain regulatory approval, it will be successfully distributed and marketed. These and other risks and uncertainties that we face are described in our most recent Annual Report on Form 10-K, filed with the Securities and Exchange Commission (SEC) on February 20, 2018, and in other filings that we make with the SEC from time to time.

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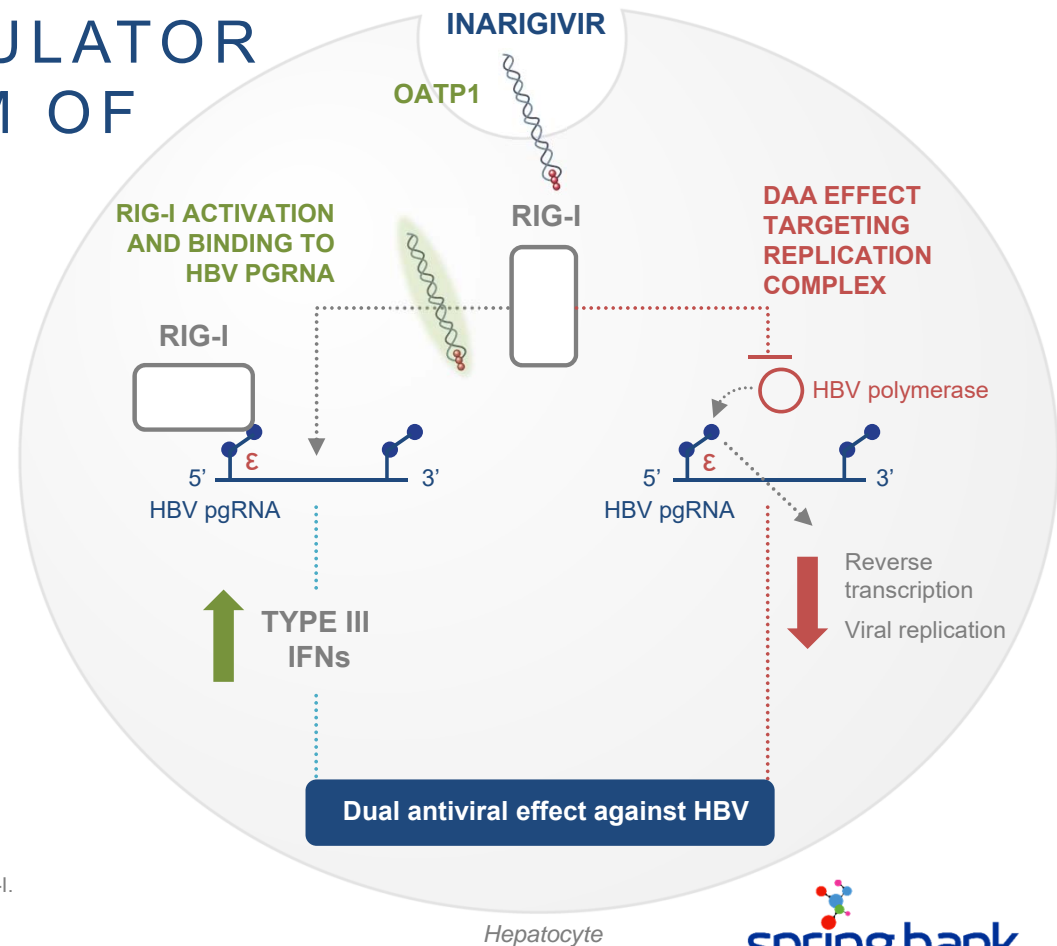
INARIGIVIR ACHIEVE TRIAL RESULTS AND HBV CLINICAL PROGRAM UPDATE

- Dose dependent responses in Cohort 3 in the ongoing ACHIEVE Trial
- Best HBsAg responder rate (28%) for oral therapies in HBV development space
- Gilead has expanded the inarigivir + Vemlidy® collaboration with Spring Bank
- Expanding and accelerating the clinical program to address multiple HBV patient populations
- Cohort 4 (200mg) has completed the majority of its enrollment and is anticipated will complete monotherapy dosing by end of 2018

INARIGIVIR: A NOVEL, ORAL SELECTIVE IMMUNOMODULATOR WITH A DUAL MECHANISM OF ACTION

INARIGIVIR is a RIG-I AGONIST which is designed to:

- **Restore hepatic selective innate and adaptive immune response** stimulating the production of type I and III IFNs
- Inhibit the HBV replication complex via a direct acting anti-viral effect
- Result in significant anti-HBV activity with reduction in HBV DNA, HBV RNA, HBsAg and cccDNA



HBV, hepatitis B virus; IFN, interferon; pgRNA, pregenomic RNA; RIG-I, retinoic acid-inducible gene-I.

Sato et al. *Immunity*. 2015;42:123-132.

INARIGIVIR – MOA STUDIES INDICATE KEY ROLE FOR SELECTIVE HEPATIC IMMUNO-MODULATION

PRE-CLINICAL DATA

- Inarigivir binds to CARDs and regulatory domain of RIG-I with activation of IRF-3 and hepato-selective innate immune response
- Inarigivir up-regulates intra-hepatic RIG-I, activates intra-hepatic ISGs and suppresses HBsAg, HBV DNA, HBV RNA and cccDNA in the woodchuck model

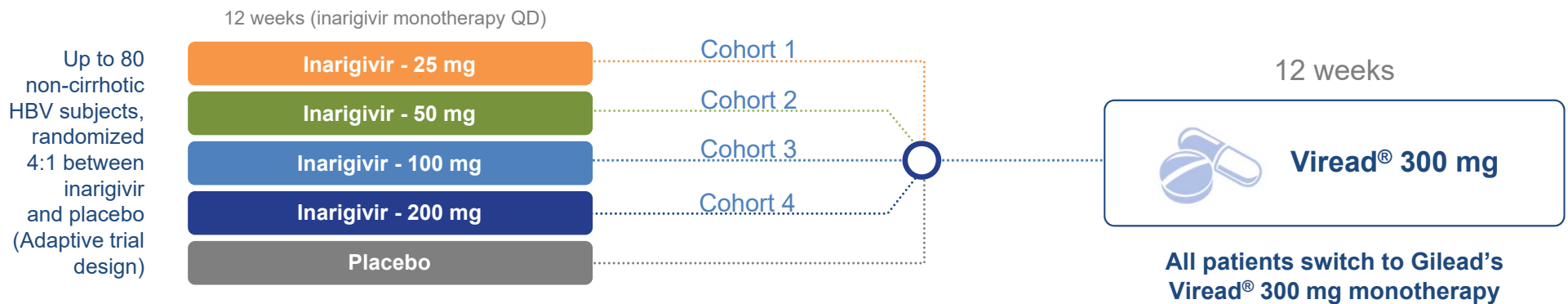
CLINICAL

- Inarigivir potent antiviral against HCV with response proportional to ISG activation and IL-28b status
- Preliminary data shows inarigivir responses in HBV associated with peripheral IP-10 reduction and activation of ISGs in PBMCs
- Inarigivir activates a B-cell neutralizing HBsAb response in responder patients

CLINICAL STUDIES OF INARIGIVIR IN HBV

ACHIEVE PHASE 2 (PART A) MONOTHERAPY DOSE ESCALATION STUDY

Clinical trial collaboration with Gilead to evaluate inarigivir with nucleotide analog Viread® 300 mg



PRIMARY ENDPOINT
Safety and antiviral activity at 12 weeks

SECONDARY ENDPOINT
PK, change in serum HBV DNA, HBsAg, HBV RNA and HBeAg from baseline to weeks 6, 12, 14, 16, and 24

Full results for all patients treated with inarigivir monotherapy anticipated in 2H 2018

DNA, deoxyribonucleic acid; HBeAg, hepatitis B e antigen; RNA, ribonucleic acid; HBsAg, hepatitis B surface antigen; HBV, hepatitis B virus; QD, once daily.

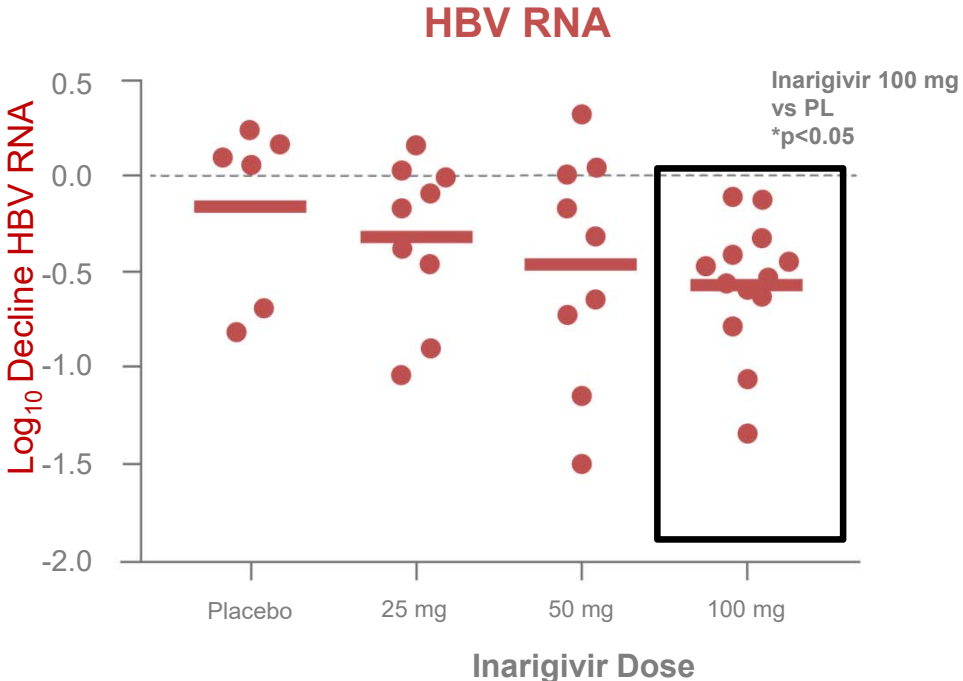
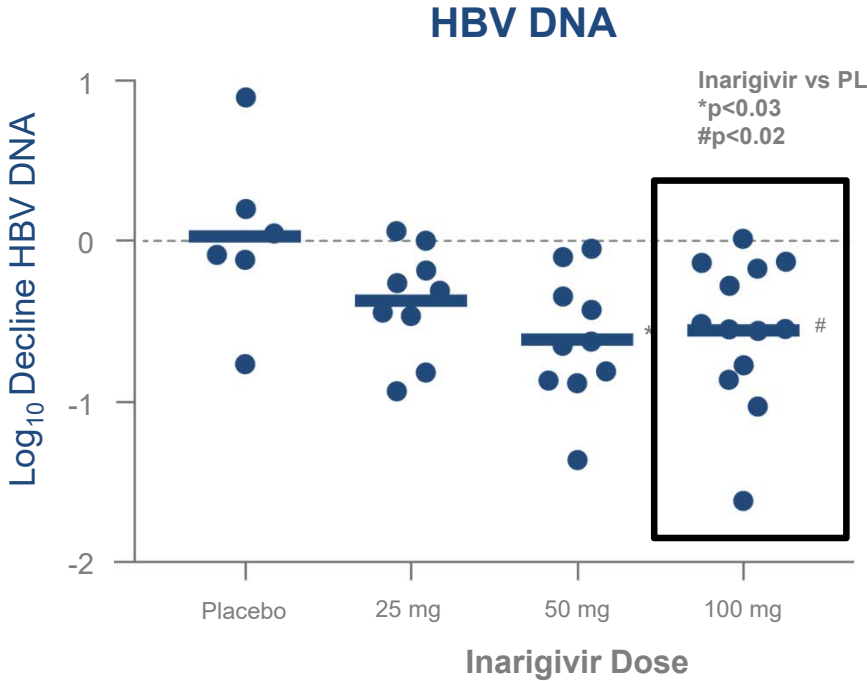
ACHIEVE STUDY BASELINE DEMOGRAPHICS

Representative demographics of the global “real world” HBV patient population

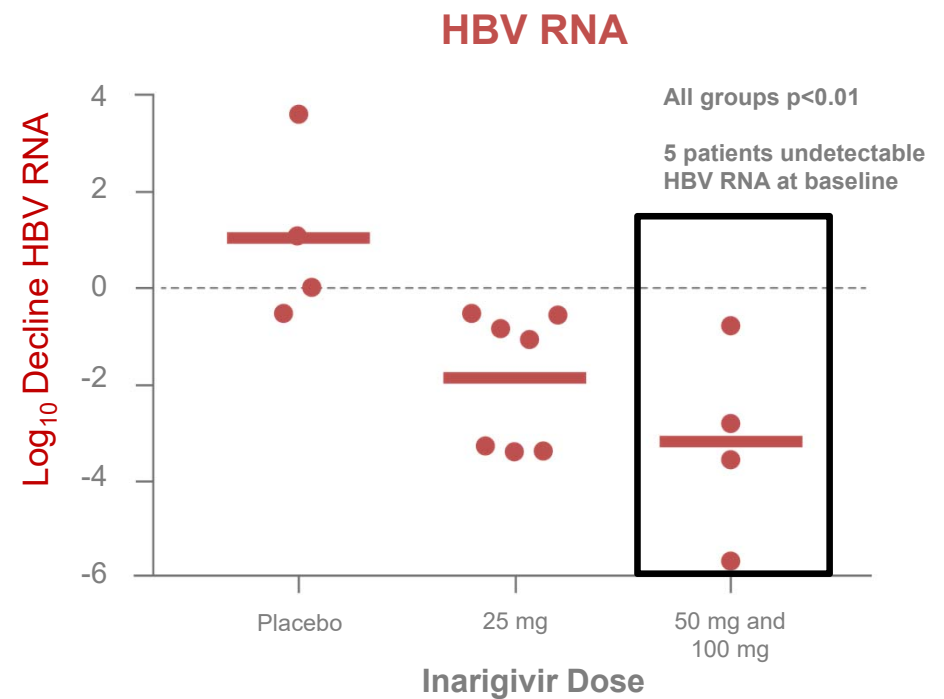
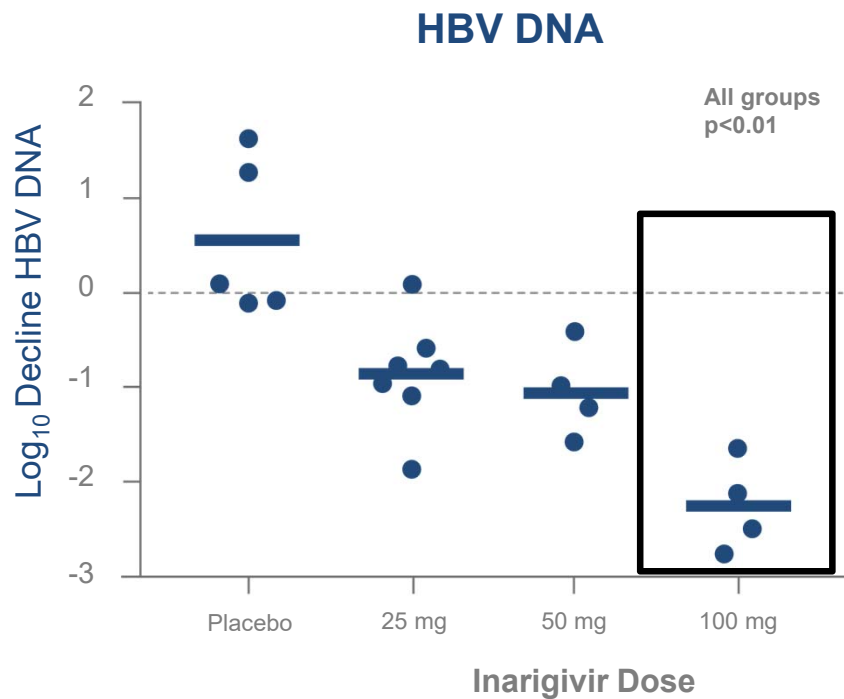
	Cohort 1			Cohort 2		Cohort 3	
	Placebo	25 mg HBeAg +ve	25 mg HBeAg -ve	50 mg HBeAg +ve	50 mg HBeAg -ve	100 mg HBeAg +ve	100 mg HBeAg -ve
Number	11	9	7	11	5	13	4
Mean Age	40	37	43	36	47	34	46
Gender M:F	7:4	5:5	3:3	9:2	5:0	7:6	3:1
Mean Baseline ALT	69	82	75	75	65	75	90
Mean Baseline HBV DNA log ₁₀	6.20	7.86	5.69	7.79	4.55	8.20	5.95
Genotype	A	1	1				
	B	6	4	3	3	4	3
	C	4	5	1	7	1	1
	D			2	1	1	

In cohort 2 (50 mg), two patients (1 HbeAg +ve and 1 HBeAg -ve) withdrew at day 1 and day 14 from patient choice

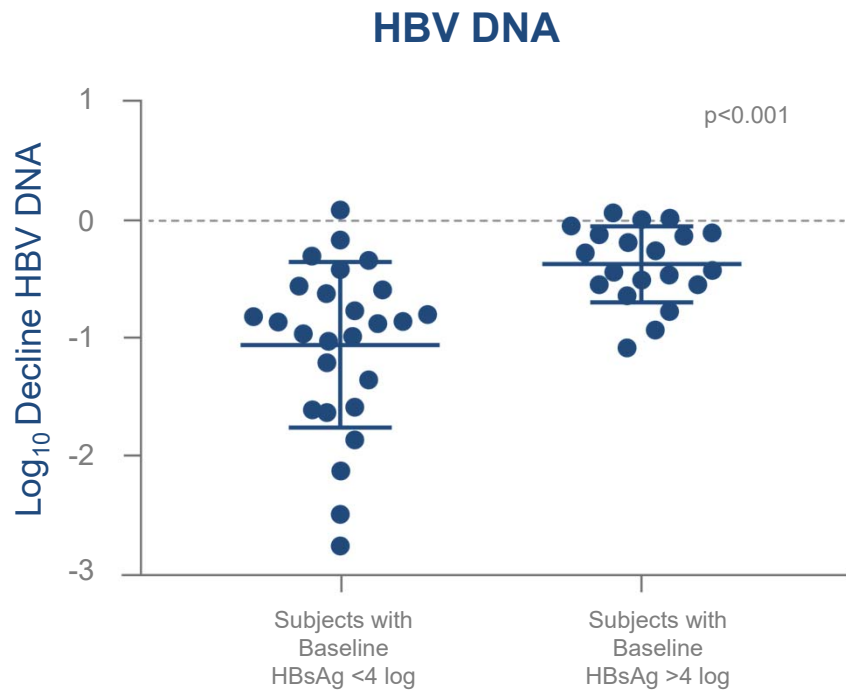
INARIGIVIR DEMONSTRATES A CONTINUING POSITIVE DOSE RESPONSE IN HBeAg +VE PATIENTS AT WEEK 12



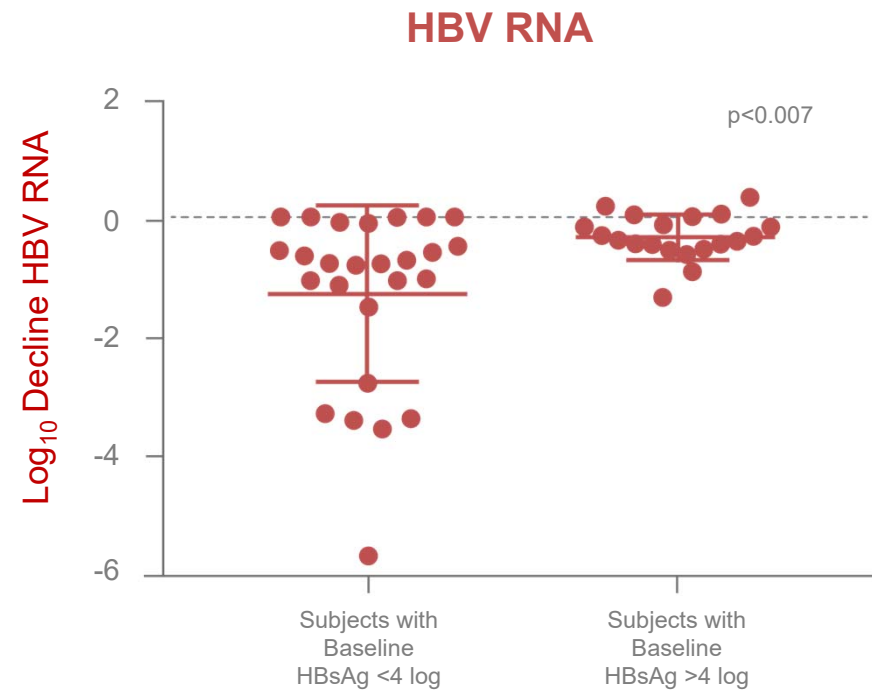
INARIGIVIR DEMONSTRATES A CONTINUING POSITIVE DOSE RESPONSE IN HB_eAg -VE PATIENTS AT WEEK 12



IN ALL COHORTS: BASELINE HBsAg PREDICTS RESPONSE OF BOTH DNA AND RNA TO INARIGIVIR



Patients: HBsAg <4 log: 16 HBeAg -ve, 10 HBeAg +ve



HBsAg >4 log: 1 HBeAg -ve, 19 HBeAg +ve

SUMMARY OF ACHIEVE PHASE 2 DATA FROM COHORTS 1,2 and 3 ON HBsAg

- Only oral drug to demonstrate meaningful clinical effect on HBsAg
- Overall, 13 of 47 (28%) patients experienced a 0.5 log₁₀ reduction on inarigivir alone or at 24 weeks after TDF switch
- Mean HBsAg reduction 0.8 log₁₀ (range 0.5 – 1.4 log₁₀) in 13 responder patients
- Effect on HBsAg seen at all doses in both monotherapy and after TDF switch
- HBsAg response seen in 7 HBeAg +ve and 6 HBeAg –ve patients across all genotypes

EFFECT OF ORAL APPROVED OR INVESTIGATIONAL HBV DRUGS ON HBsAg

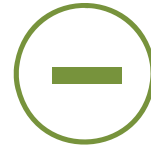


Inarigivir

Week 12 or 24 mean reduction: 0.8 log₁₀ in responder population

- No other oral drug has shown this level of decline

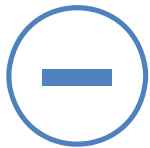
13 of 47 (28%) patients achieved at least a 0.5 log reduction, superior to any other oral HBV drug in development



TLR-7 (Vesatolimod 4 mg)

Week 12 mean reduction:
0.05 log₁₀

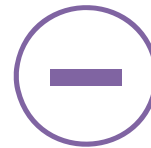
No patient >0.5 log₁₀ reduction



TDF / TAF

Week 48 mean reduction:
HBeAg +ve 0.3 log₁₀
HBeAg -ve 0.017 log₁₀

<1% HBsAg loss



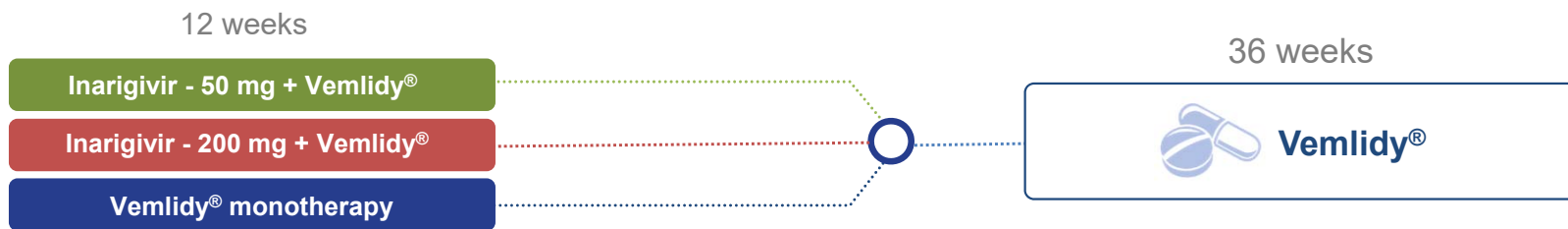
cPAM/CAPSID

No effect reported on HBsAg at week 4

GLOBAL HBV CLINICAL COLLABORATION WITH GILEAD

Expanded Gilead Phase 2 HBV Study

Inarigivir co-administered with Vemlidy® (tenofovir alafenamide) 25 mg in *naïve patients*



Initiated by
Gilead in 1Q
2018 (currently
enrolling)

Inarigivir monotherapy in *virally suppressed patients*



Executed and
funded by Gilead

INARIGIVIR DEVELOPMENT PLAN ACCOUNTS FOR HBV HETEROGENEITY



- 70-80% of chronic HBV patients
- Dominant population in US & EU
- Older age group
- Lower viral burden



- 20-30% of chronic HBV patients
- Younger population
- High viral burden

POTENTIAL MARKET ENTRY

~17 Million infected with HBV in US and EU



~12-15% Treatment rates ~10-12%

NUC-Suppressed



“Stop & Shock” Inarigivir monotherapy

OR

“Suppress & Shock” Inarigivir + existing OAV

POTENTIAL EXPANSION OPPORTUNITY

Naïve or new to treatment



Opportunity to **increase treatment rates** with improved functional cure



SB 9225
(inarigivir + TDF)



SB 9225 + siRNA

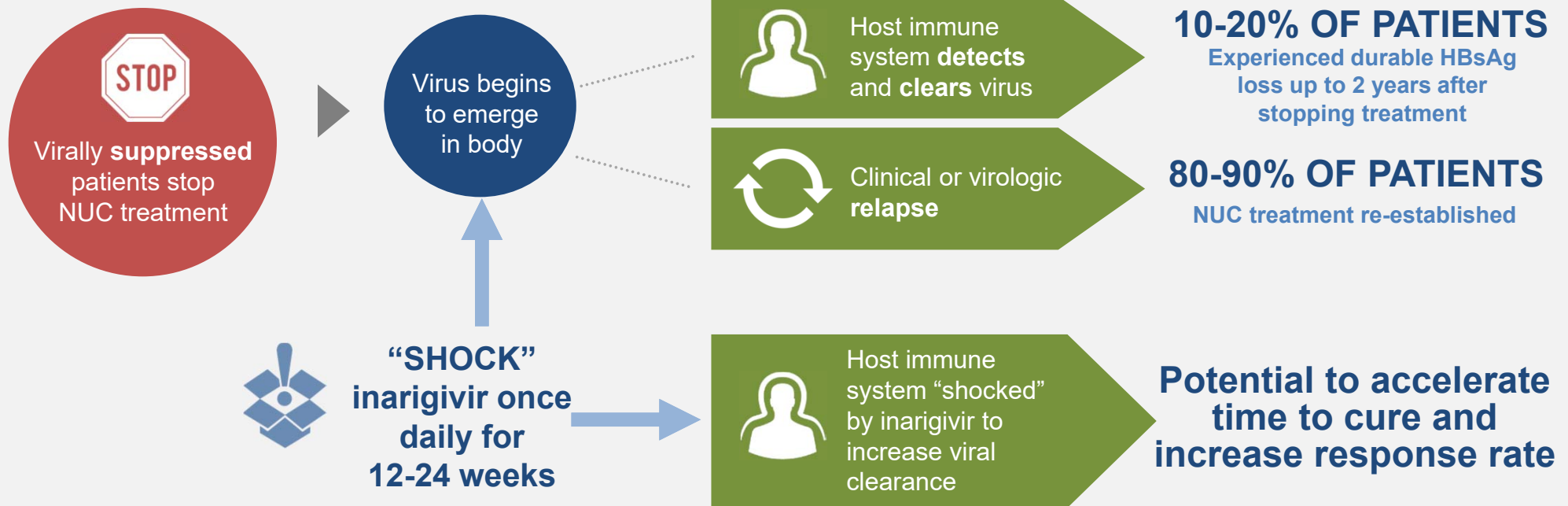
or



SB 9225 + different MOA

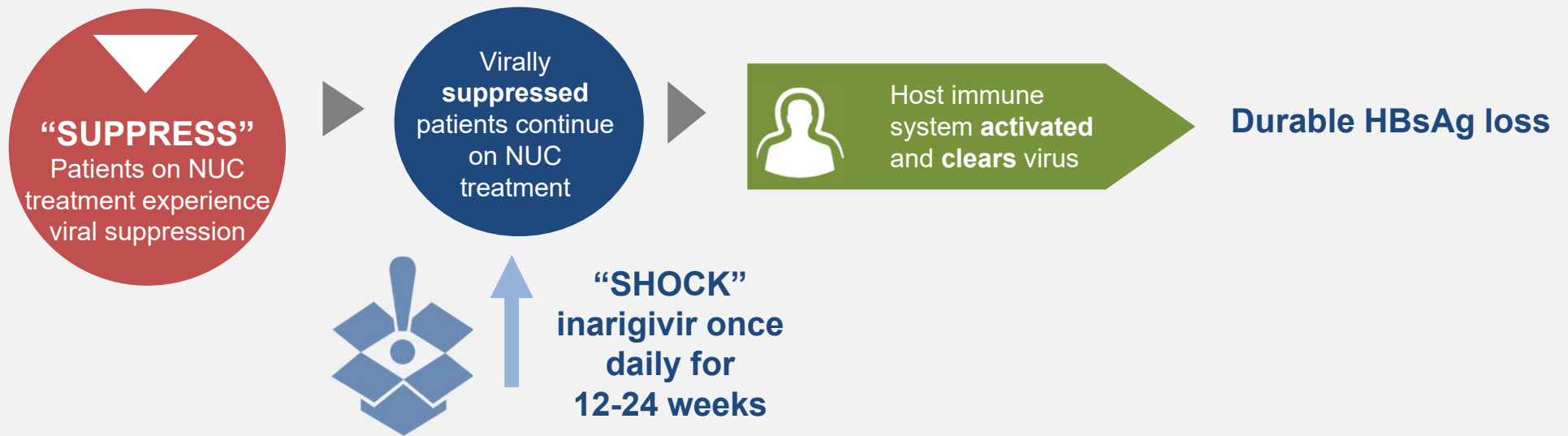
“STOP & SHOCK” – INARIGIVIR MONOTHERAPY

Inarigivir monotherapy anticipated to be studied in a Phase 2b/3 trial for its potential to improve current functional cure rate (10-20%) and reduce relapse rates following cessation of SOC therapies



“SUPPRESS & SHOCK” ADDING INARIGIVIR IN VIRALLY SUPPRESSED PATIENTS

Inarigivir immunomodulation anticipated to be studied in a Phase 2b/3 trial for its ability to promote HBsAg loss in NUC-suppressed patients



SB 9225 – FIXED-DOSE COMBINATION FOR NAÏVE HBV

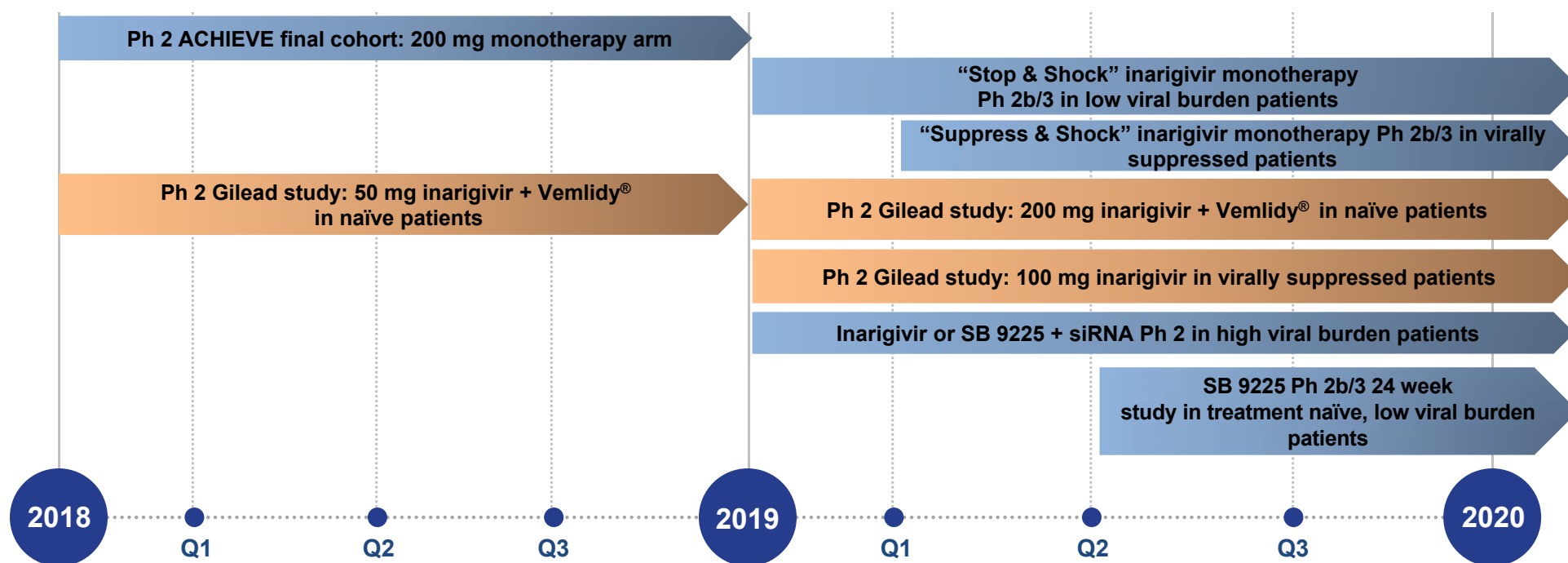
SB 9225 (inarigivir + TDF)

- Ph 2b/3 program in US, EU and ASIA (anticipated Q3 2019)
 - Newly diagnosed chronic HBV patients
 - SB 9225 once-daily vs. TDF alone
 - 24 week duration of treatment
 - Primary endpoints: HBV DNA & durable HBsAg loss

SB 9225 + siRNA / other MOA – *addressing HBsAg high viral burden population*

- Ph 2 program (anticipated early 2019)

INARIGIVIR and SB 9225 LEADING THE WAY AS BACKBONE FOR HBV DEVELOPMENT – PLANNED CLINICAL STUDIES



INARIGIVIR ACHIEVE TRIAL RESULTS AND HBV CLINICAL PROGRAM UPDATE

- Patient convenience and safety are critical to success in HBV
 - Inarigivir is a once daily oral therapy with a demonstrated favorable safety profile in the clinic
- Dose dependent responses in Cohort 3 in the ongoing ACHIEVE Trial
 - Maximum reduction in HBV DNA up to $2.76\log_{10}$ and HBV RNA up to $5.0\log_{10}$
 - 28% responder rate for HBsAg decline across all three cohorts
- Continuing evidence of immune activation by inarigivir in HBV patients
 - Experts agree that a functional cure to HBV will require immunomodulation
- Gilead has expanded the clinical collaboration with Spring Bank
 - Accelerating our expansive clinical development program