Forward Looking Statements

This presentation includes forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. Forward-looking statements include, among other things, statements, other than historical facts, regarding: the progress, scope, duration or results of clinical trials and preclinical studies of inarigivir soproxil (“inarigivir”), SB 9225, SB 11285 or any of our other product candidates or programs, such as the size, design, population, conduct, cost, objective or endpoints of any clinical trial, or the timing for initiation or completion of or availability of results from any clinical trial; the potential benefits that may be derived from any of our product candidates; our future operations, financial position, revenues, costs, expenses, uses of cash, capital requirements or our need for additional financing; or our strategies, goals, milestones, prospects, beliefs, intentions, plans, expectations, forecasts or objectives. Words such as “anticipates,” “believes,” “plans,” “expects,” “projects,” “future,” “intends,” “may,” “will,” “should,” “could,” “estimates,” “predicts,” “potential,” “continue,” “guidance,” and similar expressions sometimes identify forward-looking statements. Any forward-looking statement involves known and unknown risks, uncertainties and other factors that may cause our actual results, levels of activity, performance or achievements to differ materially from those expressed or implied by such forward-looking statement, and, therefore, you are cautioned not to place undue reliance on any forward-looking statement. These factors include, but are not limited to: whether our cash resources will be sufficient to fund our continuing operations for the period anticipated; the components, timing, costs and results of our clinical trials, preclinical studies and other development activities involving 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 9225, 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 9225, 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 March 11, 2019, and in other filings that we make with the SEC from time to time.

All forward-looking statements speak only as of April 12, 2019 and should not be relied upon as representing our views as of any other date. We specifically disclaim any obligation to update any forward-looking statement, except as required by applicable law. All trademarks, service marks, trade names, logos and brand names identified in this presentation are the properties of their respective owners.

This presentation also contains estimates and other statistical data generated by independent parties and by us relating to market size and statistics. These estimates involve a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates.
Background

• Achievement of “Functional Cure” in HBV requires:
  • Loss of HBsAg or sustained suppression of HBV DNA off all treatment after a finite duration of therapy
  • Safety and tolerability profile similar to NUCs
  • Immune control of cccDNA / HBV replication - critical for achieving a sustained response

• Inarigivir ( IRIG ) is being developed as an oral immunomodulatory backbone agent for combination strategies to achieve HBV Functional Cure
Inarigivir Acts Through Modulation of the Innate Immune System Involving RIG-I

**Novel mechanism of action**

- Actively transported into hepatocytes via OATP-1 and OAT-1 with 30:1 liver to plasma ratio
- Binds to RIG-I and causes induction of IFN signaling
- Demonstrated activation of immune system in HCV patients and healthy volunteers at 400mg daily
- DAA effect to prevent interaction of HBV Pol and pgRNA in cell systems
- Active against polymerase and capsid resistant strains
- Activates “host” targets instead of viral targets – potential for higher barrier to viral resistance

**RIG-I is a sentinel protein involved in the body’s innate defense system**
Healthy Volunteers Trial Design

Inarigivir 400 mg /Daily

<table>
<thead>
<tr>
<th>Day 1</th>
<th>Day 12</th>
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<td>11 Days 400 mg</td>
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<table>
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12 days: 14 healthy volunteers

Cytokines in sera (IFN-a, IP-10, TNF-a, IFN-g, IL-6, IL-12p70)
PBMC for flow cytometry analysis (T, NK, myeloid cells activation)
PBMC for Nanostring analysis

**Inarigivir, a RIG-I agonist, activates innate immunity in healthy volunteers.** Nina Le Bert¹, Kamini Kunasegaran¹, Meiyin Lin¹, Kevin Leach², Radhakrishnan Iyer², Antonio Bertoletti¹, Nezam Afdhal²; ¹Duke-NUS Medical School, Emerging Infectious Diseases Program, Singapore, Singapore; ²Spring Bank Pharmaceuticals, Hopkinton, United States
Evidence of Immune Activation without Systemic Cytokine Toxicity

- Serum cytokines levels of IFN-a, IFN-g, TNF-a, IL-6 and IL-12p70 were undetectable while IP-10 levels declined after inarigivir treatment.
- As early as 2h post treatment, phenotypic analysis showed **uniform** up-regulation of activation markers on monocytes (CCR2, CD16, CD86) and dendritic cells (CD86).
- The frequency of peripheral NK and CD8+ T cells declined and was associated with reduction of activating receptor NKG2D (NK cells) and increase of activation markers CD39 and HLA-DR (T cells).
- PBMC gene induction of innate immune markers was demonstrated by nanostring analysis.
- Measurements of immune cell activation before and after the first and final dose demonstrated a similar response with no evidence of tolerance.

**Inarigivir, a RIG-I agonist, activates innate immunity in healthy volunteers.** Nina Le Bert¹, Kamini Kunasegaran¹, Meiyn Lin¹, Kevin Leach², Radhakrishnan Iyer², Antonio Bertoletti¹, Nezam Afdhal²; ¹Duke-NUS Medical School, Emerging Infectious Diseases Program, Singapore, Singapore; ²Spring Bank Pharmaceuticals, Hopkinton, United States.
Inarigivir Cross-Resistance Studies

- Inarigivir effective against all known NUC resistant variants
- Inarigivir effective against pre-core mutation stop codon G1896A
- Inarigivir effective against all known capsid resistance variants

- Inarigivir will cover pre-existing NUC / CpAM variants and prevent emergent resistance variants

The Novel Antiviral Agent Inarigivir Inhibits Both Nucleos(t)ide Analogue and Capsid Assembly Inhibitor Resistant HBV in vitro. Danni Colledge¹, Kathy Jackson¹, Vitina Sozzi¹, Xin Li¹, Michael Beard², Nicholas Eyre², Junjie Zhang³, Haitao Guo³, Nezam Afdhal⁴, Radhakrishnan Iyer⁴, Stephen Locarnini¹; ¹Victorian Infectious Diseases Reference Laboratory, Melbourne, Australia; ²The University of Adelaide, Adelaide, Australia; ³Indiana University School of Medicine, Indianapolis, United States; ⁴Spring Bank Pharmaceuticals, Hopkinton, United States
ACHIEVE Phase 2 Dose Escalation Study

Inarigivir monotherapy 12 weeks followed by switch to Tenofovir 300mg for 12 weeks

Up to 80 non-cirrhotic HBV subjects, randomized 4:1 between inarigivir and placebo

12 weeks (inarigivir monotherapy QD)

- Inarigivir - 25 mg
- Inarigivir - 50 mg
- Inarigivir - 100 mg
- Inarigivir - 200 mg
- Placebo

Cohort 1
Cohort 2
Cohort 3
Cohort 4

12 weeks

Tenofovir 300 mg

All patients switch to tenofovir 300 mg monotherapy

Safety and antiviral activity at 12 weeks

PK, change in serum HBV DNA, HBsAg, HBV RNA and HBeAg from baseline to weeks 6, 12, 14, 16, and 24
## Mean Baseline Demographics by IRIG Dosing Cohort and HBeAg Status

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<tr>
<th></th>
<th>Pbo Epos</th>
<th>Pbo ENEG</th>
<th>E+ve 25mg</th>
<th>E-ve 25mg</th>
<th>E+ve 50mg</th>
<th>E-ve 50mg</th>
<th>E+ve 100 mg</th>
<th>E-ve 100 mg</th>
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<th>E-ve 200 mg</th>
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</table>

* 9 HBeAg negative patients had undetectable HBV RNA at baseline
Primary Endpoint: Mean Change from Baseline in HBV DNA at Week 12 in Placebo (PL) and IRIG Cohorts

![Bar chart showing mean change in HBV DNA from baseline at week 12 across different doses of IRIG. The x-axis represents IRIG dose (mg) ranging from PL to 200 mg, and the y-axis represents the log10 mean change. The chart indicates that as the dose increases, the mean change decreases, with placebo showing a small negative change and the 200 mg dose showing a substantial negative change.]
HBeAg-Positive Patients: Change from Baseline in HBV DNA at Week 12 and Week 24

Log₁₀

Week 12 PL or IRIG
Week 24 TDF 300mg
Mean change (per cohort)
P < 0.01: IRIG 50, 100 and 200mg vs PL
HBeAg-Negative Patients: Change from Baseline in HBV DNA at Week 12 and Week 24

18 of 22 (82%) patients undetectable at week 24
Secondary Endpoint: Mean Change from Baseline in HBV RNA at Week 12 in Placebo (PL) and IRIG Cohorts

Log$_{10}$

-0.1

-1.0

-0.8

-0.81

-1.14

PL  25mg  50mg  100mg  200mg

IRIG DOSE
HBeAg-Positive Patients: Change from Baseline in HBV RNA at Week 12 and Week 24

Log$_{10}$

-6  -4  -2  0  2

PL  25mg  50mg  100mg  200mg  PL  25mg  50mg  100mg  200mg

WEEKS 0 – 12  TDF 300mg switch

WEEKS 12 - 24

Week 12 PL or IRIG

Week 24 TDF 300mg

Mean change (per cohort)

P< 0.01: IRIG 50, 100 and 200mg vs PL
HBeAg-Negative Patients: Change from Baseline in HBV RNA at Week 12 and Week 24

All IRIG patients at 50, 100 and 200mg became undetectable at week 12

P =0.05: All cohorts combined versus PL at week 12

3 placebo and 6 IRIG undetectable HBV RNA at baseline. 1 placebo became replicative and detectable at week 12
Baseline HBsAg Cutoff of $4\log_{10}$ Predictor of HBV DNA and HBV RNA Response to IRIG at Week 12

Change from Baseline to Week 12 $\log_{10}$

- HBV DNA
- HBV RNA
- Mean change

$P < 0.001$ for both HBV DNA and HBV RNA

24 HBeAg +ve and 1 HBeAg -ve $< 4\log_{10}$
16 HBeAg +ve and 21 HBeAg -ve $< 4\log_{10}$
Positive Predictors of Response for IRIG

- **HBV DNA and HBV RNA**
  - Baseline HBsAg $< 4\log_{10}$
  - Baseline IP-10 $> 310\text{ng/L}$
  - Reduction in IP-10 $> 110\text{ng/L}$ between baseline and week 12

- **HBsAg**
  - Genotype B $> C$
  - Good responses genotype A / D but numbers small
Secondary Endpoint: Predefined Responders with HBsAg Reduction of $\geq 0.5\log_{10}$

<table>
<thead>
<tr>
<th></th>
<th>Week 12 $&gt;0.5\log_{10}$</th>
<th>Week 24 $&gt;0.5\log_{10}$</th>
<th>Total Responders</th>
<th>Notes</th>
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</thead>
<tbody>
<tr>
<td>Placebo /TDF</td>
<td>1*</td>
<td>2*</td>
<td>2</td>
<td>*ALT flare $&gt;400$ IU/ml</td>
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<td>IRIG 25mg/TDF</td>
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<td>8</td>
<td>#2 non sustained of which 1 dose reduced</td>
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<td>IRIG 50mg/TDF</td>
<td>1$^\S$</td>
<td>2</td>
<td>2</td>
<td>$^\S$1 non sustained and dose reduced</td>
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<td>IRIG 100mg/TDF</td>
<td>1</td>
<td>2</td>
<td>2</td>
<td>1 non-sustained with a flare</td>
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<tr>
<td>IRIG 200mg/TDF</td>
<td>1</td>
<td>3</td>
<td>3</td>
<td>2 GT C patients</td>
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</table>

- 16 IRIG patients (26%) met predefined HBsAg loss criteria for response at week 12 or 24
- Response in 7 HBeAg negative (mean $0.7\log_{10}$) and 9 HBeAg positive (mean $0.9\log_{10}$)
- Overall mean responder reduction of $0.8\log_{10}$ (range 0.5 – $1.4\log_{10}$)
Quantitative HBsAg Responder Patients > 0.5$\log_{10}$ Reduction at Week 12 or Week 24 from Baseline

Mean Change in HbsAg
Week 12: 0.4$\log_{10}$
Range 0.1 – 0.9$\log_{10}$

Week 24: 0.72$\log_{10}$
Range 0.15 - 1.4$\log_{10}$
HBsAg Response (> 0.5$log_{10}$) by Genotype

HBsAg change in $log_{10}$

Percentage of responders within each Genotype

- GT A 100%
- GT B 33%
- GT C 10%
- GT D 75%

Genotype response data consistent with that seen with IFN therapy
Preliminary Safety Analysis

- Most common mild / moderate TEAE’s all groups
  - Headache / dizziness 13; fatigue 9; abd pain/GI upset 10;
  - Flu / flu like symptoms 5 URTI 10; ALT / AST elevation: 8
- 1 Grade 3 transient hypertriglyceridemia not sustained on retesting
- 1 SAE of hospitalization for knee pain, patient on placebo in cohort 4
- No investigator determined interferon-like side effects
- No difference between active Rx or placebo and no dose dependency
- 3 patients discontinued
  - 1 placebo after hospitalization for knee pain
  - 2 in 50mg group withdrew consent at Day 1 and Day 14 for patient preference
Conclusion

- IRIG demonstrated dose dependent responses for HBV DNA and HBV RNA
- Baseline HBsAg major predictor of HBV DNA and HBV RNA response
- HBsAg response seen in 26% of patients at either 12 or 24 weeks
  - Responders seen at every dose and may indicate response more dependent on host immunity
  - More common in Genotype B versus C
- Safety profile excellent with good tolerability and no systemic interferon like effects
- IRIG can be considered as a backbone immunomodulator in combination studies with agents having different MOAs