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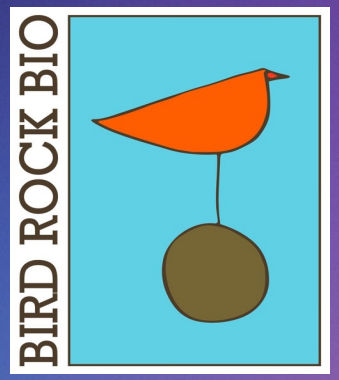


# Transaction & Overview

Q3 2023

# FORWARD LOOKING STATEMENTS

This presentation contains "forward-looking statements", including statements regarding Skye Bioscience, Inc. ("Skye Bioscience and/or the Company"), within the meaning of the "safe harbor" provisions of the Private Securities Litigation Reform Act of 1995. All statements in this presentation, whether written or oral, that are not descriptions of historical facts or that refer to expected or anticipated future actions and results of Skye Bioscience are forward-looking statements, including statements regarding Skye Bioscience's cash runway, anticipated timelines, and milestones with respect to product development programs, business strategy, expected plans with respect to clinical trials, including the timing of patient enrollment and clinical trial data updates, and commercialization, if ever, of endocannabinoid system-targeting and CB1-targeting therapeutics. In addition, any statements that refer to expectations, projections or other characterizations of future events or circumstances are forward-looking statements. Forward-looking statements can be identified by terminology including "anticipated," "plans," "goal," "focus," "aims," "intends," "believes," "can," "could," "challenge," "predictable," "will," "would," "may" or the negative of these terms or other comparable terminology. Forward-looking statements reflect our current projections and expectations about future events as of the date of this presentation and involve known and unknown risks, uncertainties and other factors that may cause the actual results, performance or achievements to be materially different from those expressed or implied by the forward-looking statements, including those uncertainties and factors described in Skye' Bioscience's most recent Annual Report on Form 10-K filed with the Securities and Exchange Commission and our subsequent periodic reports filed with the Securities and Exchange Commission.

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# TRANSACTION HIGHLIGHTS

**$17M institutionally-led financing**

- $12 M PIPE led by 5AM Ventures; joined by Versant Ventures and another investor
- $5 M convertible note

**Bird Rock Bio acquisition**

- $20 M merger consideration for Bird Rock's outstanding equity interests held by dedicated biotechnology investors exchanged for Skye common stock

**Management and board of directors**

- Existing Skye management team will continue to lead the company
- Existing board of directors expanded with addition of Andy Schwab (Managing Partner, 5AM Ventures) and Paul Grayson (Venture Partner, Versant & CEO,Tentarix)

**Primary use of proceeds**

- SBI-100 OE glaucoma: prepare/report Phase 1 data for SBI-100 OE in Q3; start Phase 2a enrollment in Q4; interim Phase 2a data 1H '24
- Develop nimacimab Phase 2 clinical strategy for chronic kidney disease. Initiate Phase 2a H1 2024
- Expected cash runway into 2024.

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BIRD ROCK BIO

# FIRST- & ONLY-IN-CLASS PHASE 2-READY CLINICAL ASSETS

## NIMACIMAB

- **CB1 inhibitor (negative allosteric modulator)**
- **Nimacimab: monoclonal antibody**
  - Inhibits ligand-mediated and intrinsic CB1 signaling
  - **Highly selective** for CB1, with no detectable binding for CB2 or other GPCRs
  - **Mechanism of action** in fibrotic, inflammatory and metabolic diseases
- Completed 3-week and 26-week toxicology studies with up to 75 mg/kg administered by-weekly sub-cutaneously in cynomolgus monkeys
- Completed Phase 1 SAD study in healthy volunteers and MAD in non-alcoholic fatty liver disease (NAFLD) and diabetic kidney disease (DKD) patients
- Open INDs for chronic kidney disease, NASH, gastroparesis

## SBI 100 OE

- **CB1 activator (agonist)**
- **SBI-100 OE: small molecule prodrug** of natural cannabinoid
  - CB1 receptors **highly expressed in the eye** and known to be involved in reducing intraocular pressure
  - **Highly selective for CB1**, with no detectable binding of CB2 or other GPCRs
  - **Mechanism of action** in inflammation and neuroprotection
- Completed 14-day toxicology studies with up to 2% concentration administered daily topically in two different species
- Completed Phase 1 SAD/MAD and starting Phase 2a proof-of-concept study in glaucoma patients
- Open IND for glaucoma

# PROFORMA CAPITALIZATION (Unaudited)

| Proforma Cap Table | 8/18/2023 | Post-Reverse Split[3] |
|---|---|---|
| **Common shares outstanding** | **3,078.1 M** | **12.3 M** |
| Options and RSUs | 38.0 M | 0.2 M |
| Warrants | 821.2 M | 3.3 M |
| Convertible note (as-converted basis)[1 2] | 242.2 M | 0.9 M |
| **Common shares fully diluted** | **4,179.5 M** | **16.7 M** |
| **Transaction[2]** | | |
| **Merger consideration** | **$19.9 M** | |
| Common shares | 968.0 M | 3.9 M |
| **PIPE financing** | **$12.0 M** | |
| Common shares | 1,138.5 M | 8.3 M |
| Warrants | 581.4 M | 2.2 M |
| **10% Short-term convertible note** | **$5.0 M** | |
| Common shares (as-converted basis) | 242.2 M | 0.9 M |
| Warrants | 85.0 M | 0.3 M |

- Shares of Skye common stock issued to Bird Rock stockholders in exchange for 100% of Bird Rock's outstanding equity interest
- Common shares issued to investors (including certain Bird Rock stockholders) in $12 million private placement
- Post-deal Skye to have >65% institutional ownership
  - 5AM Ventures
  - Versant Ventures
  - Other specialist life science investors
- Please refer to the company's SEC filings for additional information.

*[1] 85 million warrants issued exercisable at deal price related to convertible note (included in warrant total)*
*[2] Subject to 12-month lock-up*
*[3] Pending FINRA approval*

# ADVANCING DISTINCT CB1-TARGETING THERAPEUTICS

## Skye has two clinical-stage programs with multiple clinical inflection points

### NIMACIMAB

| MOA | Disease | R&D | Phase 1 | Phase 2 |
|---|---|---|---|---|
| CB1 Receptor Inhibitor *Sub-cutaneous* | Chronic Kidney Disease | | | |

### SBI-100 OE

| MOA | Disease | R&D | Phase 1 | Phase 2 |
|---|---|---|---|---|
| CB1 Receptor Agonist *Topical* | Glaucoma | | | |

**Best-in-class and Only-in-class Molecules**

**Nimacimab** – only CB1 negative allosteric modulator antibody in the clinic
**SBI-100 OE** – first/only prodrug of THC developed and currently in the clinic for glaucoma

**Validated Targets/ Clear Clinical Endpoints**

**Nimacimab** – proteinuria is an accepted surrogate for demonstrating improved kidney function for proof-of-concept
**SBI-100** – lowering intraocular pressure (IOP) prevents subsequent progression of functional damage in the retina and is accepted as an approvable clinical endpoint

**Favorable Safety Profiles**

Both drugs designed to minimize safety issues associated with previous CB1 modulators, while maximizing clinical benefit of targeting this axis for disease modification.

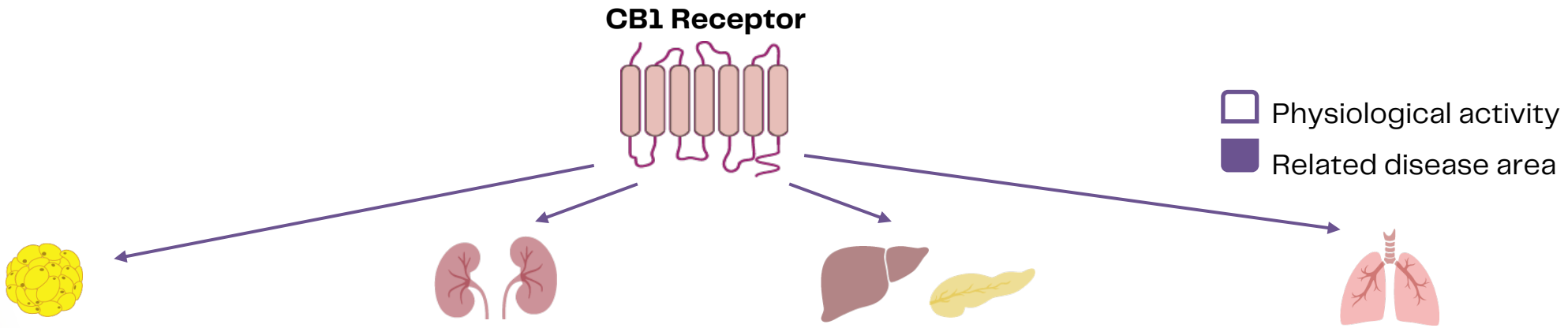
# EXPLOITING PROVEN TARGETS WITH IMPROVED DRUG DESIGN

## CB1 is a validated target for glaucoma and other inflammatory/fibrotic/metabolic diseases

| Dynamics | Nimacimab | SBI-100 OE |
|---|---|---|
| **Basic Goal** | Reduce inflammatory, fibrotic and/or metabolic processes that cause other degenerative conditions in organs. | Reduce intraocular pressure in the eye. Potentially provide neuroprotection of optical nerve cells |
| **History** | Rimonabant validated CB1 receptor as effective target for obesity | Cannabis/THC known to reduce intraocular pressure since 1970s. Also known to protect against neurodegeneration. |
| **Historic Challenge** | Safety – depression due to CNS exposure | Safety – psychotropic effects due to CNS exposure, coupled with poor bioavailability in ocular tissue |
| **Skye Improvements** | New mechanism for CB1 inhibition: negative allosteric modulator<br>Highly selective for CB1 receptor in the periphery (i.e. outside the brain); is not detected in CNS<br>PK profile allows for favorable dosing regimen | Local delivery with eye drop in a novel formulation<br>Prodrug design for improved bioavailability in the eye<br>Designed for minimal/no psychotropic effect |

# CB1 OVERACTIVATION: ROLE IN CRITICAL DISEASES

## Upregulation of CB1 signaling involved in multiple inflammatory, fibrotic and metabolic diseases in various organs; significant prevalence and unmet needs




| Adipose Tissue | Kidneys | Liver & Pancreas | Lungs |
|---|---|---|---|
| ↑De novo fatty acid synthesis<br>↑Triglyceride accumulation<br>↓Lipolysis | ↑ Inflammation<br>↑ Fibrosis | ↑ De novo lipogenesis<br>↓ Insulin signaling<br>↑ Fibrosis | ↑ Inflammation<br>↑ Fibrosis |
| **Metabolic Disorders/ Obesity** | **Chronic Kidney Disease** | **Metabolic Disorders/ Diabetes** | **Pulmonary Fibrotic Disease** |

# COMPETITIVE LANDSCAPE VALIDATING CB1 MOA

## Nimacimab sets itself apart from other CB1 peripherally-targeting agents

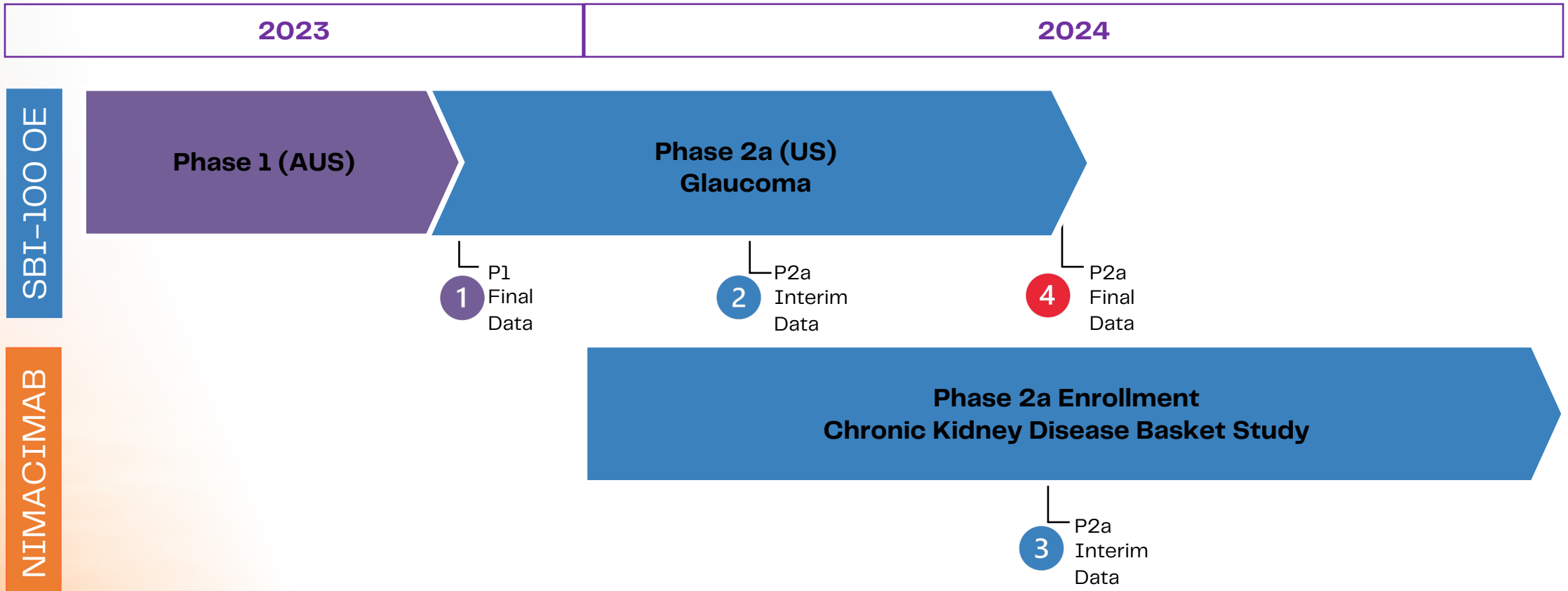
| | GFB-024 | INV-202 | NIMACIMAB |
|---|---|---|---|
| **Molecule Type** | Antibody | Small Molecule | Antibody |
| **Allosteric Modulator** | ○ | ○ | ✓ |
| **Inverse Agonist** | ✓ | ✓ | ○ |
| **Favorable Safety**<br>Phase 1 data | ✓ | ✓ | ✓ |
| **No CNS Accumulation**<br>Based on preclinical data | ✓ | ○ | ✓ |
| **Immunogenicity**<br><20%ADA | ○ | N/A | ✓ |

inversago PHARMA

**Recently acquired by Novo Nordisk for $1.075B based on positive Phase 1 data of INV-202**

# ANTICIPATED CLINICAL MILESTONES

## Working toward four data catalysts in two key programs over the next two years



# LEADERSHIP

## Contributed to commercialization of 47+ drugs/diagnostics, led high-value strategic transactions and co-founded multiple companies

### Executive Management

**Punit Dhillon**
*CEO & Chair of BOD*

**Tu Diep, MSc**
*Chief Development Officer*

**Chris Twitty, PhD**
*Chief Scientific Officer*

**Kaitlyn Arsenault, CPA**
*Chief Financial Officer*

### Board of Directors

**Andy Schwab**
*Managing Partner, 5AM Ventures*

**Deborah Charych, PhD**
*Co-founder and former CTO, RayzeBio*

**Keith Ward, PhD**
*Founder, Pres./CEO, & Chair, Kuria Therapeutics*

**Paul Grayson**
*Pres./CEO, Tentarix Bio; Versant partner*

**Praveen Tyle, PhD**
*Founder, Potens Pharma*

**Margaret Dalesandro, PhD**
*Pharma. Dev. Consultant, Brecon Pharma Consulting*

# COMPELLING VALUE PROPOSITION

## Advancing two Phase 2 programs targeting cannabinoid receptor 1 (CB1)

| | |
|---|---|
| PATIENTS FIRST | Purpose statement: Guided by scientific excellence, Skye pioneers new medicines, leveraging the endocannabinoid system with the sole purpose of transforming the lives of patients facing devastating diseases |
| NOVEL TECHNOLOGY | Portfolio of two distinct first-in-class, ***only-in-class*** CB1-targeting technologies:<br>• SBI-100 OE: CB1 agonist/activator focused on glaucoma/ocular hypertension<br>• Nimacimab: CB1 inhibitor to treat fibrotic, metabolic, and inflammatory diseases such as chronic kidney disease and NASH |
| EXPERIENCED TEAM | Expert board of directors, management and scientific advisors to pursue exit opportunity for product(s) and company |
| INTELLECTUAL PROPERTY | Robust intellectual property and R&D pipeline to expand product pipeline and complement development strategy |
| CLINICAL MILESTONES | Multi-compound endocannabinoid system-targeting development pipeline strategy with milestones from three separate studies over 18 months |
| COMMERCIAL POTENTIAL | Significant market opportunity for each indication in development; multiple billions in aggregate addressing significant, distinct commercial opportunities |

# SKYE NEXT STEPS

## Achieve SBI-100 OE/glaucoma proof-of-concept milestone; advance nimacimab into clinic with longer-term view toward franchise expansion

- SBI-100 OE Phase 1 glaucoma clinical data Q3 2023
- SBI-100 OE Phase 2a glaucoma clinical trial first dosing Q4 2023
- Nimacimab Phase 2a chronic kidney disease clinical trial initiation Q1 2024
- Continued in vivo studies, biomarker development, next-generation
- Planned SBI-100 OE Phase 2b glaucoma clinical trial initiation 2024
- Following P2a proof of concept for nimacimab, potential for clinical expansion to additional inflammatory, metabolic and fibrotic disorders
- Maintain focused operational and clinical development strategy
- Selectively evaluate business development opportunities to advance product pipeline
- Plan R&D Day in fall of 2023