NEUROCRINE® BIOSCIENCES

Neurocrine Biosciences 2023 Analyst Day

December 5, 2023

NEUROCRINE® BIOSCIENCES

Dr. Kevin Gorman

CHIEF EXECUTIVE OFFICER

Neurocrine Biosciences Attendees

Kevin Gorman, Ph.D.
Chief Executive Officer

Matt Abernethy
Chief Financial Officer

Eric Benevich
Chief Commercial Officer

David Boyer
Chief Corporate Affairs Officer

Julie Cooke
Chief Human Resources Officer

Ingrid Delaet, Ph.D.
Chief Regulatory Officer

Kyle Gano, Ph.D.
Chief Business Development & Strategy Officer

Dimitri E. Grigoriadis, Ph.D.
Chief Research Officer

Darin M. Lippoldt
Chief Legal Officer

Jude Onyia, Ph.D.
Chief Scientific Officer

Eiry Roberts, M.D.
Chief Medical Officer

NEUROCRINE BIOSCIENCES

Agenda

TIME (EST PM)	Topic	Speaker(s)
1:00 – 2:00	Welcome / CEO Opening Remarks	Kevin Gorman
(R&D Focus)	R&D Vision and Strategy	Jude Onyia
	R&D Q&A Session	Jude Onyia, Eiry Roberts, Kyle Gano, Jerold Chun, Grace Liang
2:00 – 3:15	A Brief History of CRF	Kevin Gorman / Dimitri Grigoriadis
(CAH Focus)	Congenital Adrenal Hyperplasia (CAH) Overview	Eiry Roberts
	CAH Panel	Moderated by Jean Chan and Bob Farber with Guest Panelists
	Crinecerfont Phase 3 Results	Eiry Roberts
	CAH / Crinecerfont Q&A Session	Guest Panelists, Eiry Roberts, Jean Chan, Bob Farber
3:15 – 3:45	CEO Closing Remarks / Open Q&A Session	Kevin Gorman / All
3:45 – 4:45	**Webcast Concludes / Breakout Sessions Begin**	
(Breakouts)	- Track A: R&D Strategy and Vision	Jude Onyia, Kyle Gano, Jerold Chun, Grace Liang
	- Track B: CAH / Crinecerfont	KOLs, Jean Chan, Bob Farber, Matt Abernethy, Eric Benevich
	- Track C: Psychiatry / Muscarinic Compounds	Eiry Roberts, Jaz Singh, Samir Siddhanti
4:45 – 5:00	Post-Breakout Networking / Analyst Day Concludes	All

Forward-Looking Statements

In addition to historical facts, this presentation contains forward-looking statements that involve a number of risks and uncertainties. These statements include, but are not limited to, statements regarding the potential benefits to be derived from certain of our product candidates and our future development plans. Among the factors that could cause actual results to differ materially from those indicated in the forward-looking statements include: our future financial and operating performance; risks and uncertainties associated with the commercialization of our products; the risk that our products and/or product candidates will not be found to be safe and/or effective or may not prove to be beneficial to patients; that development activities for our products and/or product candidates may not be completed on time or at all; risks that clinical development activities may be delayed for regulatory or other reasons, may not be successful or replicate previous and/or interim clinical trial results, or may not be predictive of real-world results or of results in subsequent clinical trials; risks that regulatory submissions for our products and/or product candidates may not occur or be submitted in a timely manner; risks that our products and/or product candidates may not obtain regulatory approvals; or that the U.S. Food and Drug Administration or regulatory authorities outside the U.S. may make adverse decisions regarding our products and/or product candidates; risks and uncertainties relating to competitive products and technological changes that may limit demand for our products; risks associated with our dependence on third parties for development and manufacturing activities related to our products and our product candidates, and our ability to manage these third parties; and other risks described in the Company's periodic reports filed with the Securities and Exchange Commission, including without limitation the Company's quarterly report on Form 10-Q for the quarter ended September 30, 2023. Neurocrine Biosciences disclaims any obligation to update the statements contained in this presentation after the date hereof.

Where Are We Today?

- **Discovered and Developed** Three Novel FDA-Approved Programs
- **Deep Expertise** in Neuroscience Drug Development
- **Fully-Integrated Organization** with Both R&D and Commercial Capabilities
- **Growing Blockbuster** Commercial Product in INGREZZA with Strong IP Protection
- **Future Blockbuster Opportunity** with Crinecerfont
- **Largest Portfolio of Muscarinic Compounds** in Clinical Development
- **Strong Financial Profile** That Can Support Significant R&D Investment

Neurocrine Biosciences Has Unparalleled Scale and Focus

NEUROCRINE™ BIOSCIENCES

Building and Maximizing the Pipeline

of Programs by Stage

Phase 1	Phase 2	Phase 3	NDA
5	8	4	1

			Phase 1	Phase 2	Phase 3	NDA	Milestone
Neurology							
valbenazine*	*Sprinkle Formulation*	*VMAT2 Inhibitor*					PDUFA: 4/30/2024
valbenazine*	*Dyskinetic Cerebral Palsy*	*VMAT2 Inhibitor*					Phase 3 Ongoing
NBI-827104[2]	*EE-CSWS*	*Ca_v 3.1, 3.2, 3.3*					Phase 2 Ongoing
NBI-921352[3]	*SCN8A-DEE*	*Na_v1.6*					Phase 2 Ongoing
NBI-1076986	*Movement Disorders*	*M4 Antagonist*					Submitting CTA
Neuroendocrinology							
crinecerfont[4]	*CAH: Adults*	*CRF-R1*					NDA: 2024
crinecerfont[4]	*CAH: Pediatrics*	*CRF-R1*					NDA: 2024
Efmody	*Adrenal Insufficiency*	*GC Receptor*					Phase 2 Data: 1H '24
Efmody	*CAH*	*GC Receptor*					Phase 2 Data: 1H '24
Neuropsychiatry							
valbenazine*	*ATS*	*VMAT2 Inhibitor*					Phase 3 Ongoing
NBI-1065845[5]	*Inadequate Response-MDD*	*AMPA*					Phase 2 Data: 1H '24
luvadaxistat[5]	*CIAS*	*DAAO*					Phase 2 Data: 2H '24
NBI-1117568[1]	*Schizophrenia*	*M4 Agonist*					Phase 2 Data: 2H '24
NBI-1070770[5]	*MDD*	*NMDA NR2B NAM*					Phase 2 Initiating
NBI-1117570[1]	*CNS Indications*	*M1/M4-Dual*					Phase 1 Ongoing
NBI-1117569[1]	*CNS Indications*	*M4-Preferring*					Phase 1 Ongoing
NBI-1117567[1†]	*CNS Indications*	*M1-Preferring*					Phase 1 Initiating
NBI-1065890	*CNS Indications*	*VMAT2 Inhibitor*					Submitting CTA

NEUROCRINE BIOSCIENCES

* Mitsubishi Tanabe Pharma Corporation (MTPC) has commercialization rights in Japan and other select Asian markets

† Sosei Heptares has retained rights in Japan; Neurocrine Biosciences may opt-in to a 50:50 cost and revenue share upon certain development events

In-licensed program =
(1) Sosei Heptares (2) Idorsia Ltd (3) Xenon Pharmaceuticals Inc (4) Sanofi
(5) Takeda Pharmaceutical Company Ltd
Neurocrine Biosciences has global rights unless otherwise noted.

NEUROCRINE® BIOSCIENCES

Dr. Jude Onyia

CHIEF SCIENTIFIC OFFICER

R&D Vision

Top 5 Global Leadership in Neuroscience

Five Year Plan

Produce 20 Development Candidates*

- “20 in 5” Goal Will be a Product of Internal Research and External Innovation
- Will Span Range of Modalities (Small Molecules, Peptides, Antibodies, Gene Therapy)
- Increased Internal R&D Breadth and Depth Will Enhance Ability and Quality of Diligence Rigor to Assess External Opportunities

Long-Term Steady State

Produce One Commercial Product Every Two Years

- Requires Several “Shots on Goal” Per Year and Significant Investment, Leveraging Our Strong Financial Profile

NEUROCRINE BIOSCIENCES

* Development Candidate = Molecule Entering GLP Toxicology Studies (Last Stage of IND-Enabling Work)

R&D Strategy

Build Breadth and Depth

- Strengthen Therapeutic Area Expertise
- Strengthen Existing Modality + Build New Modalities
- Shift Focus to Higher Probability
  "Best & Next-In Class" Targets
- Deploy External Innovation to Accelerate R&D

Goal: Deliver A Diversified Portfolio Across Therapeutic Areas and Modalities

Committed to Improving Our Probability of Success

Focus Areas to Improve Probability of Success

Guiding Principles

Right Targets

Right Drugs

Right Patients

Deep Understanding

of Disease and Unmet Need

Clinical and / or Genetic

Validation

Translationally Relevant

Endpoints

Leverage

Shared Pathophysiological Mechanisms

Modality

Agnostic Approach

Explore Multi-Target

Drug Combinations

NEUROCRINE BIOSCIENCES

NEUROCRINE® BIOSCIENCES

Therapeutic Areas of Focus

Therapeutic Areas of Focus

Prioritizing Heavier Investment in Neurology vs. Neuropsychiatry Today

Neurology
(50%)

Neuropsychiatry
(25%)

Neuroendocrinology
(15%)

Neuroimmunology
(10%)

What Do We Want To Add Over Next Five Years?

Neurology	Neuropsychiatry	Neuroendocrinology
Movement Disorders	Schizophrenia	Congenital Adrenal Hyperplasia
Epilepsy	Depression	**Metabolic Disease**
Neuromuscular	**Bipolar Mania**	**Rare Endocrinology**
Neurodegenerative/ Neurodevelopmental	**Alzheimer's Disease Psychosis**	

Neuroimmunology Tech Platform

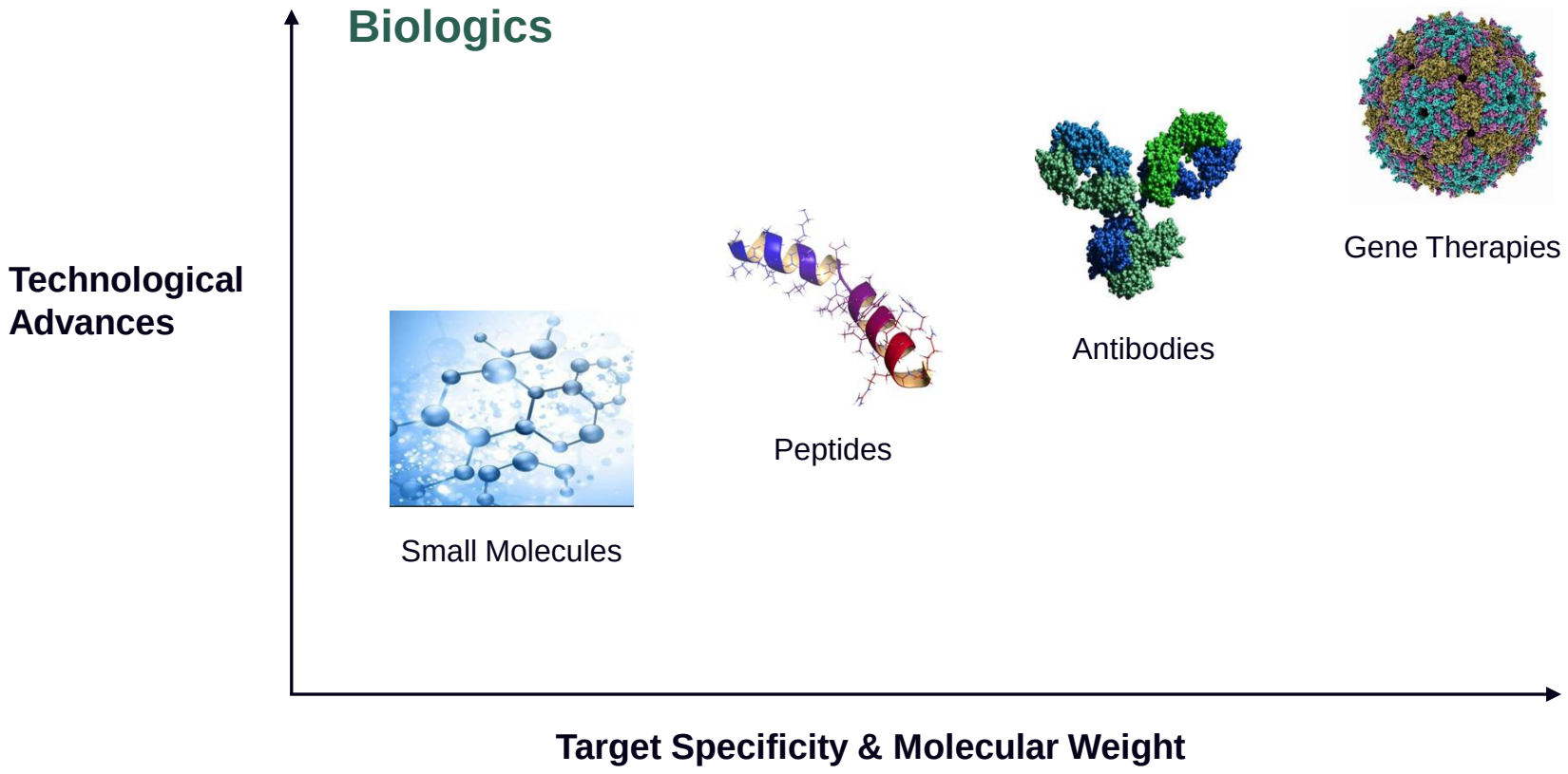
Immune-mediated Neuronal Disorders and Neurodegenerative Diseases

NEUROCRINE BIOSCIENCES

NEUROCRINE® BIOSCIENCES

Modalities

Modalities Expand the Range of Therapeutic Innovation



Science

+

Strategy

+

Investment

NEUROCRINE BIOSCIENCES

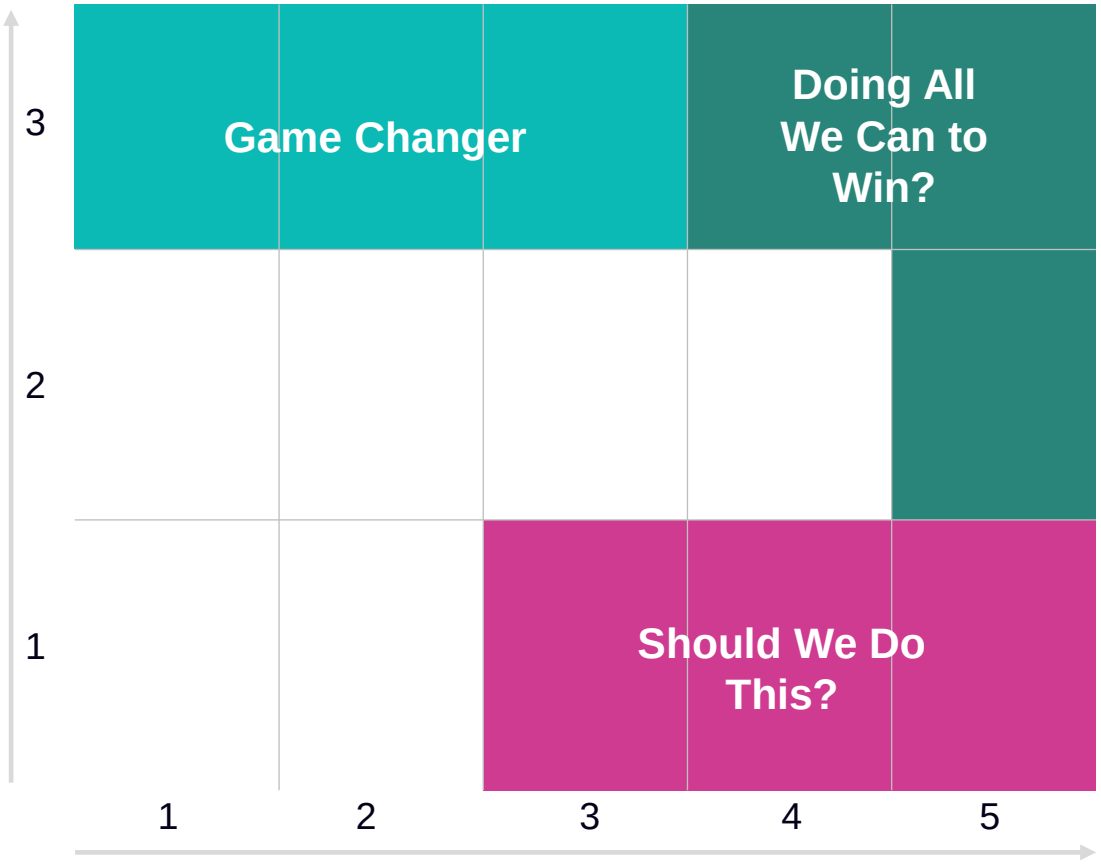
New Opportunities Via Modalities Across Therapeutic Areas

Tech Platforms

	Small Molecules	Peptides	Antibodies	Gene Therapy
Neuropsychiatry	✓	?	?	
Neurology	✓	✓	✓	✓
Neuroendocrinology	✓	✓	✓	✓
Neuroimmunology	✓	✓	✓	✓

NEUROCRINE BIOSCIENCES

Where Do We Point The Engine?



Opportunity
[Unmet Need]

Confidence / Ability to Deliver
[Biology/Chemistry/Clinical]

Focus on High Confidence and High Opportunity Targets

NEUROCRINE BIOSCIENCES

Molecule Design & Engineering

Developing a Competitive Advantage at Neurocrine Biosciences

Design Principles — Patient Outcome Centric

Maximize Efficacy

Maximize Safety

Ideal Drug-Like Profile

Convenient Delivery

EFFICACY

1) Better pharmacology
2) Added pharmacology
3) Better time action

SAFETY

1) Improve safety
2) Improve specificity
3) Reduce immunogenicity

DRUG-LIKE PROFILE

1) Improve stability
2) Improve expression
3) Improve solubility

CONVENIENT DELIVERY

1) Better formulation
2) Device compatibility
3) Compliance & outcome

Strategic Line of Sight from Concept to Patient

NEUROCRINE® BIOSCIENCES

Leveraging External Innovation as a Multiplier

Leveraging External Innovation for Over 30 Years

COMMERCIAL PRODUCT
Increase Topline Growth, Accelerate Presence in Disease States Supported by Pipeline Programs

CLINICAL-STAGE PROGRAMS
Focus on Programs with Proof-of-Concept, Expand and / our Maintain Pipeline in Core TAs

ENABLING TECHNOLOGY
Add to Early-Stage Pipeline Through Externalization – New Modalities, AI-Driven Tools, Assay & Screening Methodologies, etc.

We Remain Agnostic To Deal Structure

OPTION-TO-LICENSE FOR RISK MANAGEMENT

- Relevant for Early-Stage Deal
- Limits Neurocrine Resources Until Program Achieves Key Milestone (e.g. IND Acceptance)

ROYALTY LICENSE TO PROFIT SHARE

- Utilized Across All Areas of Interest

ACQUISITION, WITH FOCUS ON:

- Pre-Commercial to Commercial Product
- Mid-to-Late-Stage Program
- Platform Technology

Sourcing Assets and Technology is a Competitive Advantage

We Have a Unique Ability to Align Partner Needs and Interests with Our Own

Internal R&D Will Meet External Innovation to Build and Sustain Our Pipeline

Treatment	Company	Targets/Modalities	Examples
Symptomatic Treatments To Precision Medicine	abbvie, SANOFI, sosei HEPTARES	GPCRs	**Commercial:** ORILISSA®, ORIAHNN® (GnRH) **Phase 3:** Crinecerfont (CRF) **Phase 2:** NBI-'568 (Muscarinic M4) **Phase 1:** NBI-'570 (Muscarinic M1/M4 Dual)
	jnana Therapeutics, Takeda	Enzymes, Transporters	**Phase 2:** Luvadaxistat (DAAO)
	XENON, idorsia, Takeda	Ion Channels	**Phase 2:** NBI-'770 (NMDA NR2B NAM), NBI-'845 (AMPA), NBI-'104 (Ca_V3.1-3.3), NBI-'352 (Na_V1.6)
	Diurnal	Nuclear Receptors	**Commercial:** Alkindi®, Efmody®
Disease Modification To Curative Therapies	voyager THERAPEUTICS	Gene Therapies	**Preclinical:** GBA1-Parkinson's / Gaucher, Friedreich's Ataxia, Five Undisclosed Targets
New Modalities	Sentia MEDICAL SCIENCES, INC., ABLEXIS, BIOCYTOGEN, charles river, OmniAb	Peptides, Antibodies, Proteins, Delivery-Formulation Technology	**Preclinical: >10 targets including** CRF

NEUROCRINE® BIOSCIENCES

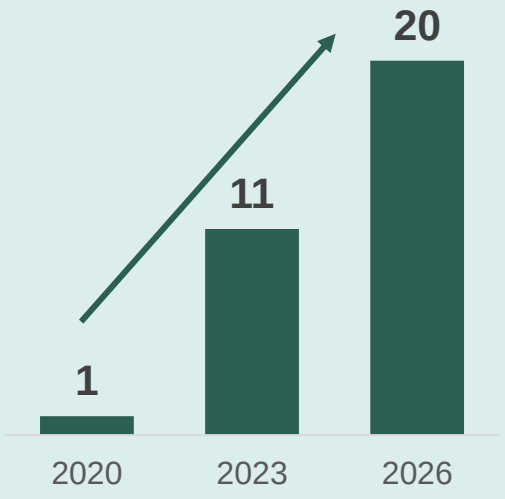
Emerging Pipeline:

Building Blocks for Rapid / Sustainable Portfolio Growth

Early R&D Trends Are Positive With Increased Number of Assets and Faster Timeframe Leading to Robust Early Clinical Pipeline

- **10 New Development Candidates since 2021**
  (Includes Internal and External Compounds)
- **6 Clinical Trial Applications / Investigational New Drug Applications**
- **Timelines Accelerated**
  from Idea to Development Candidate / First-in-Human by 25-50%
- **Advanced First Biologics Development Candidates in 2023**
  (Peptide, Antibody and Gene Therapy)
- 1-2 **Gene Therapy Programs On-Track**
  to Enter First-in-Human Studies in 2025

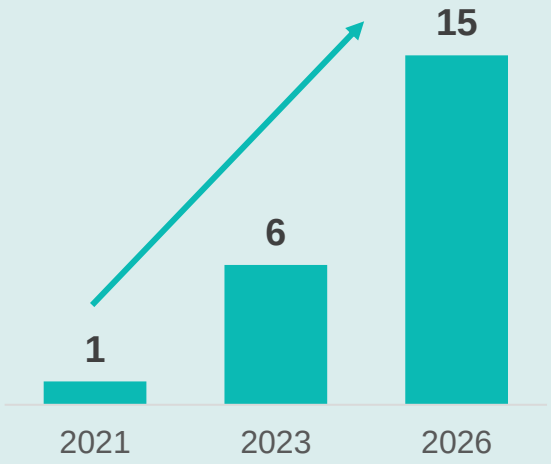
Number of Development Candidates by Year



11X Increase in 2023

20X Increase by 2026

Number of Eligible Phase 1 Candidates



6X Increase in 2023

15X Increase by 2026

NEUROCRINE BIOSCIENCES

2024 Portfolio Pipeline Snapshot

Discovery and Preclinical *Select Programs*			Clinical Development *Phase I*	*Phase II*	*Phase III*	NDA
#1	#9	#1	NBI-567 — M1 Preferring Ag	NBI-770 — NMDA NR2B NAM (Oral)	valbenazine — ATS	valbenazine — sprinkle
#2	#10	#2	NBI-569 — M4 Preferring Ag	NBI-568 — Schizophrenia	valbenazine — DCP	
#3	#11	#3	NBI-570 — M1/M4 Ag	NBI-845 — MDD	crinecerfont — CAH Adults	
#4	#12	#4	NBI-890 — VMAT2	luvadaxistat — CIAS	crinecerfont — CAH Peds	
#5	#1	#5	NBI-986 — M4 Antagonist	NBI-352 — SCN8A DEE		
#6	#2	#1		NBI-104 — CSWS		
#7	#3	#2		Efmody — AI		
#8				Efmody — CAH		

- Neurology
- Neuropsychiatry
- Neuroendocrinology
- Neuroimmunology

NEUROCRINE BIOSCIENCES

Ag = Agonist; VMAT2 = Vesicular Monoamine Transporter 2; LAI = Long-Acting Injectable' NR2B-NAM = N-Methyl-D-Aspartate Receptor Subtype 2B Negative Allosteric Modulator; MDD = Major Depressive Disorder; CIAS = Cognitive Impairment Associated with Schizophrenia; SCN8A-DEE = SCN8A Developmental and Epileptic Encephalopathy; CSWS = Epileptic Encephalopathy with Continuous Spike and Wave During Sleep; AI = Adrenal Insufficiency; ATS = Adjunctive Treatment of Schizophrenia; DCP = Dyskinetic Cerebral Palsy; CAH = Congenital Adrenal Hyperplasia; Peds = Pediatrics; HD = Huntington Disease

2024 Portfolio Pipeline Snapshot

Therapeutic Areas

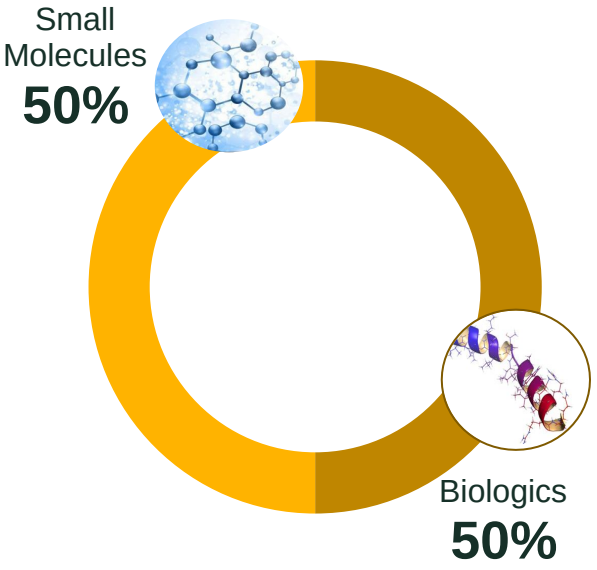
Neurology
(50%)

Neuropsychiatry
(25%)

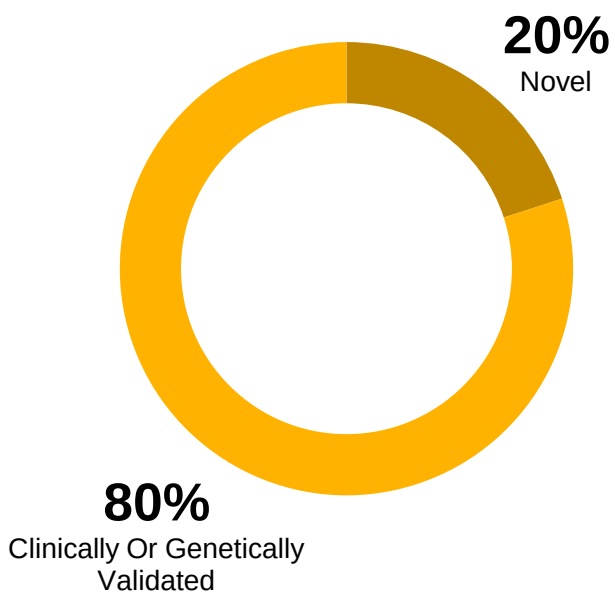
Neuroendocrinology
(15%)

Neuroimmunology
(10%)

Modalities



Targets



“Must Win” Areas of Focus

VMAT2 Inhibitors Neuropsychiatry / Neurology	CRF-R1 Antagonist Neuroendocrinology (+)	Muscarinic Programs Neuropsychiatry / Neurology	Gene Therapy Neurology
NBI-890 (Oral QD / Low Dose / LAI) VMAT2 VMAT2 (+) (Dual Pharmacology)	Crinecerfont CRF R1 Follow-On CRF CRF CRF	NBI-568 (M4 Agonist) NBI-567 (M1-Preferring Agonist) NBI-569 (M4-Preferring Agonist) NBI-570 (M1/M4 Dual Agonist) NBI-986 (M4 Antagonist)	GBA1 Parkinson’s Disease / Gaucher Disease FXN Friedreich’s Ataxia 5 Additional Pre-Clinical Programs

Our R&D Strategy Is Delivering Results

- Top Talent Bench of Chemists and Biologists in Place
- Developed Engineering Capabilities Across a Variety of Diversified Modalities
- Focused on our Core Therapeutic Areas (TAs) of Interest
- Advanced Early Portfolio is Now Diversified Across TAs and Modalities
- Pre-clinical and Development Candidate Portfolio is Growing

Neurocrine Biosciences Is Uniquely Positioned to Advance Steady Flow of Innovative Clinical Candidates to Patients Across our Neuroscience-Focused Therapeutic Areas of Interest

NEUROCRINE® BIOSCIENCES

R&D Q&A Session

NEUROCRINE® BIOSCIENCES

Dr. Dimitri Grigoriadis

CHIEF RESEARCH OFFICER

Neurocrine Biosciences: Founded on a CRF Platform

30+ years of R&D on CRF1 Receptor Antagonists for Neuroendocrine Diseases

Recent Positive Phase 3 Results for Crinecerfont in Adult AND Pediatric CAH

- 1981 CRF Identified
- Human CRF_2 Receptor Cloned 1996
- Rat CRF_2 Receptor Cloned 1995
- Human CRF_1 Receptor Cloned 1993
- **NBI** Founded **1992**
- 1st Human Trial CRF Antagonist 1998
- Phase 2 MDD 2000
- Phase 2 MDD 2003
- Phase 2 GAD 2003
- Phase 2 Anxiety 2004
- Phase 2 Endocrine Trier Stress Test 2007
- Phase 2 MDD 2010
- Phase 1 CAH 2013 NBI-77860
- Phase 1/2 CAH 2015 NBI-77860
- Phase 2 CAH 2016 NBI-77860
- IND CAH Crinecerfont 2016
- Phase 2 Adult CAH 2018
- Phase 3 Crinecerfont Adult CAH 2020
- Phase 3 Crinecerfont Ped CAH 2021
- Positive Phase 3 Adult CAH 2023
- Positive Phase 3 Pediatric CAH 2023

1992 | 1994 | 1996 | 1998 | 2000 | 2002 | 2004 | 2006 | 2008 | 2010 | 2012 | 2014 | 2016 | 2018 | 2020 | 2022 | 2024

Neurocrine Biosciences: Our History with CRF

R&D Efforts Across the Spectrum of the CRF System

GPCRs, Neuroendocrine Peptides and Binding Protein

CRF1 Receptor Antagonists

janssen	NBI-30775 | Phase 2
GSK	NBI-34041 | Phase 2
GSK	GW876008 | Phase 2
GSK	NBI-77860 | Phase 2
GSK	NBI-76169 | Phase 1
sanofi	crinecerfont | Phase 3

5

Industry-Wide Clinical Programs Discovered / Associated With Neurocrine went to Phase 2 or beyond

NEUROCRINE® BIOSCIENCES

Dr. Eiry Roberts

CHIEF MEDICAL OFFICER

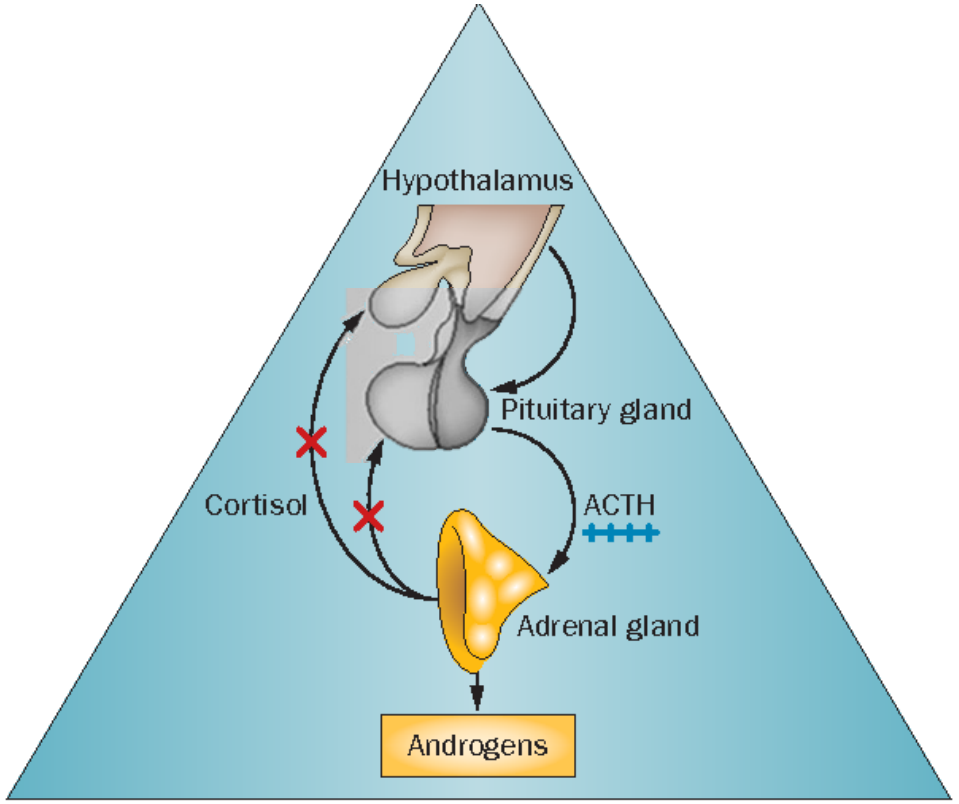
Classic Congenital Adrenal Hyperplasia Due to 21-Hydroxylase Deficiency (21OHD CAH)

21OHD CAH Results in:

- Impaired Synthesis of Cortisol and (Often) Aldosterone
- Excess Adrenal Androgen Production

Treatment Must Balance Consequences of:

- Supraphysiologic Glucocorticoid (GC) Doses
- High ACTH and Androgen Excess



Adapted from: Han TS et al. *Nat Rev Endocrinol.* 2014;10(2):115-24.

NEUROCRINE BIOSCIENCES

Mallappa A and Merke DP. *Nat Rev Endocrinol.* 2022;43(1):91-159.
ACTH, adrenocorticotropic hormone; GC, glucocorticoids; TARTs, testicular adrenal rest tumors.

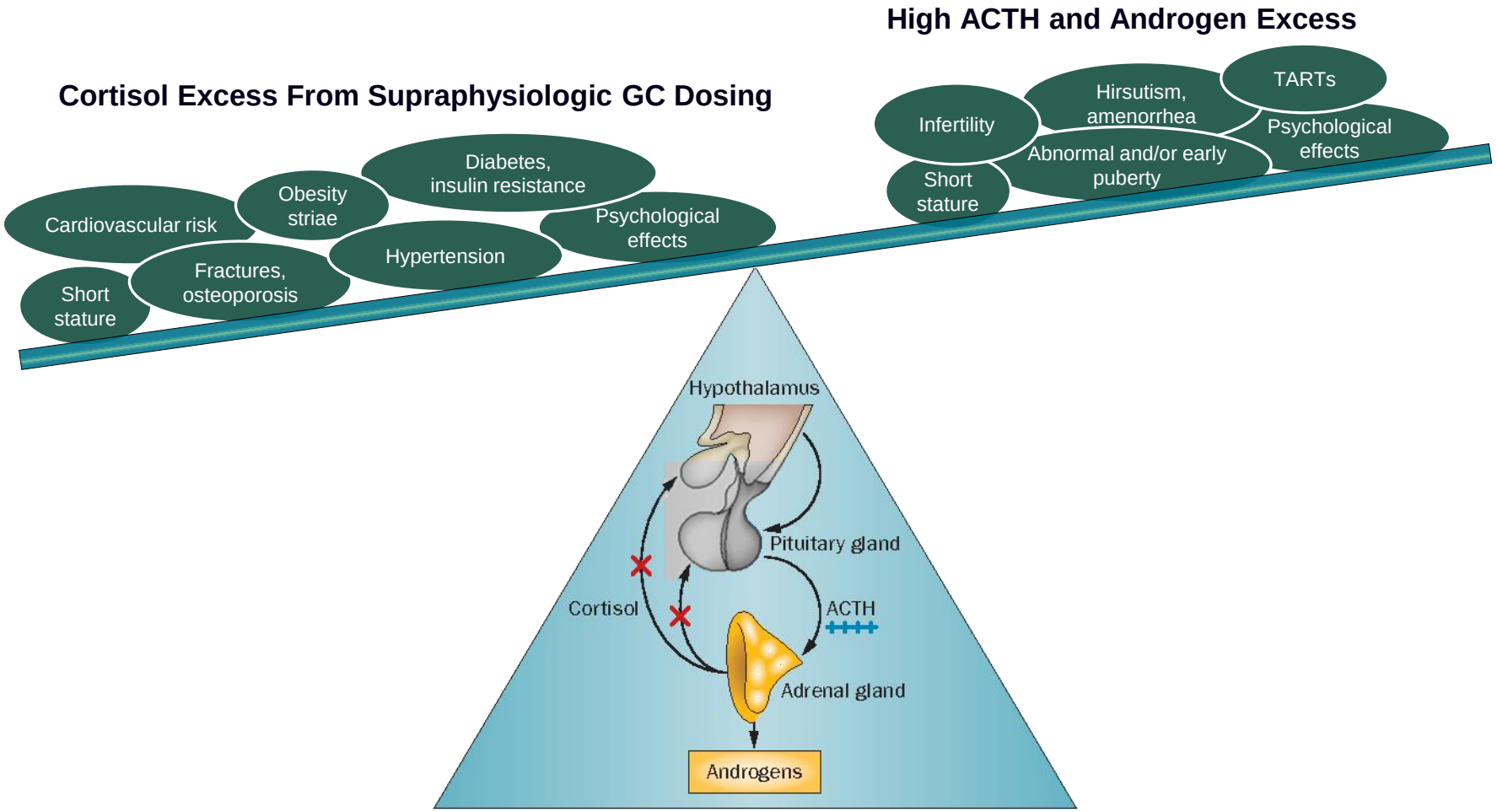
Classic Congenital Adrenal Hyperplasia Due to 21-Hydroxylase Deficiency (21OHD CAH)

21OHD CAH Results in:

- Impaired Synthesis of Cortisol and (Often) Aldosterone
- Excess Adrenal Androgen Production

Treatment Must Balance Consequences of:

- Supraphysiologic Glucocorticoid (GC) Doses
- High ACTH and Androgen Excess



Adapted from: Han TS et al. *Nat Rev Endocrinol.* 2014;10(2):115-24.

Mallappa A and Merke DP. *Nat Rev Endocrinol.* 2022;43(1):91-159.
ACTH, adrenocorticotropic hormone; GC, glucocorticoids; TARTs, testicular adrenal rest tumors.

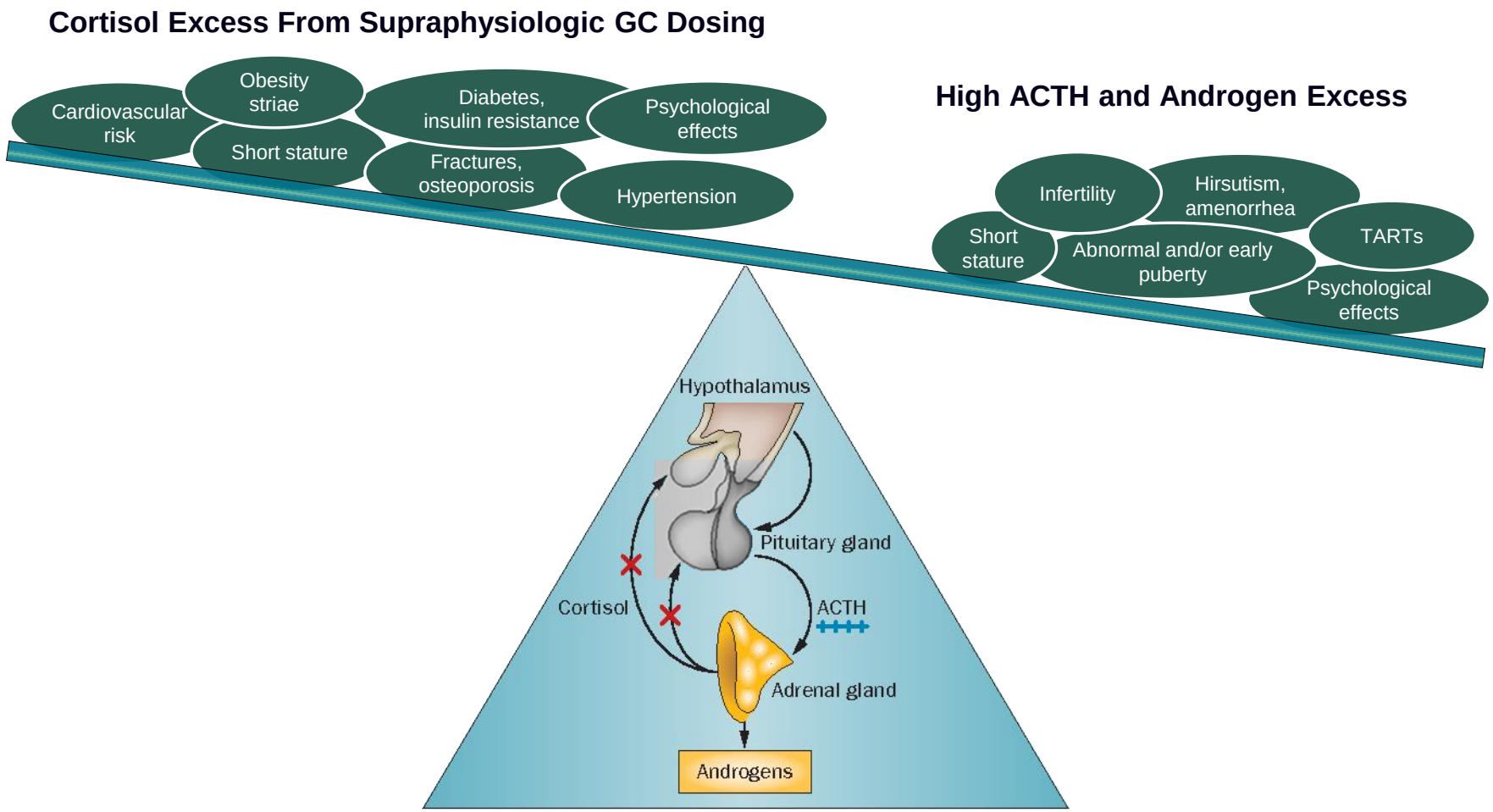
Classic Congenital Adrenal Hyperplasia Due to 21-Hydroxylase Deficiency (21OHD CAH)

21OHD CAH Results in:

- Impaired Synthesis of Cortisol and (Often) Aldosterone
- Excess Adrenal Androgen Production

Treatment Must Balance Consequences of:

- Supraphysiologic Glucocorticoid (GC) Doses
- High ACTH and Androgen Excess



Adapted from: Han TS et al. *Nat Rev Endocrinol.* 2014;10(2):115-24.

Mallappa A and Merke DP. *Nat Rev Endocrinol.* 2022;43(1):91-159.
ACTH, adrenocorticotropic hormone; GC, glucocorticoids; TARTs, testicular adrenal rest tumors.

Classic Congenital Adrenal Hyperplasia Due to 21-Hydroxylase Deficiency (21OHD CAH)

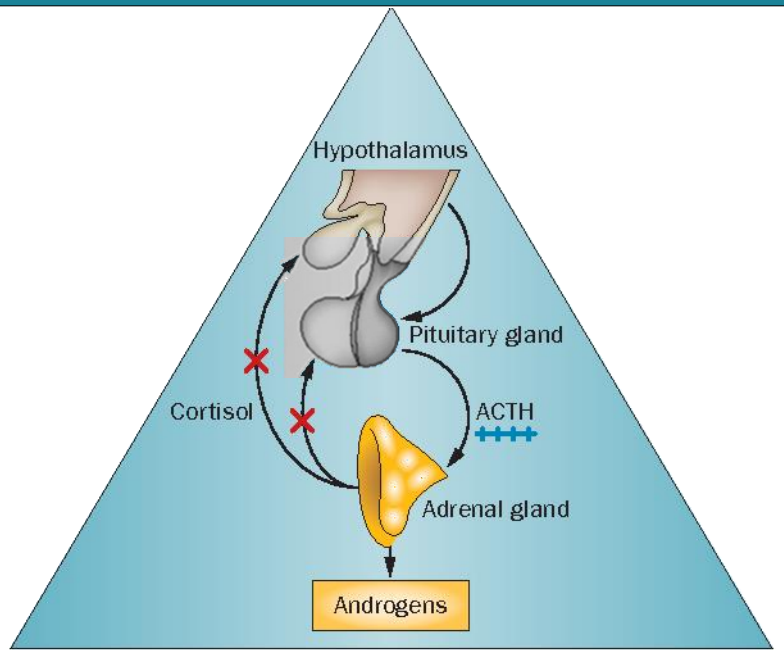
21OHD CAH Results in:

- Impaired Synthesis of Cortisol and (Often) Aldosterone
- Excess Adrenal Androgen Production

Treatment Must Balance Consequences of:

- Supraphysiologic Glucocorticoid (GC) Doses
- High ACTH and Androgen Excess

Reduced GC Dosing **crinecerfont** **Androgen Control**



Adapted from: Han TS et al. *Nat Rev Endocrinol.* 2014;10(2):115-24.

NEUROCRINE BIOSCIENCES

Mallappa A and Merke DP. *Nat Rev Endocrinol.* 2022;43(1):91-159.
ACTH, adrenocorticotropic hormone; GC, glucocorticoids; TARTs, testicular adrenal rest tumors.

NEUROCRINE® BIOSCIENCES

CAH Panel Discussion

MODERATED BY JEAN L. CHAN AND BOB FARBER

Congenital Adrenal Hyperplasia Panelists

Richard Auchus, M.D., Ph.D.
University of Michigan
(Adult Endocrinologist, CAH Expert)

Kyriakie Sarafoglou, M.D.
University of Minnesota
(Pediatric Endocrinologist, CAH Expert)

Dina Matos
Executive Director,
CARES Foundation

Lesley Holroyd
CAH Patient Advocate,
CARES Foundation Board Member

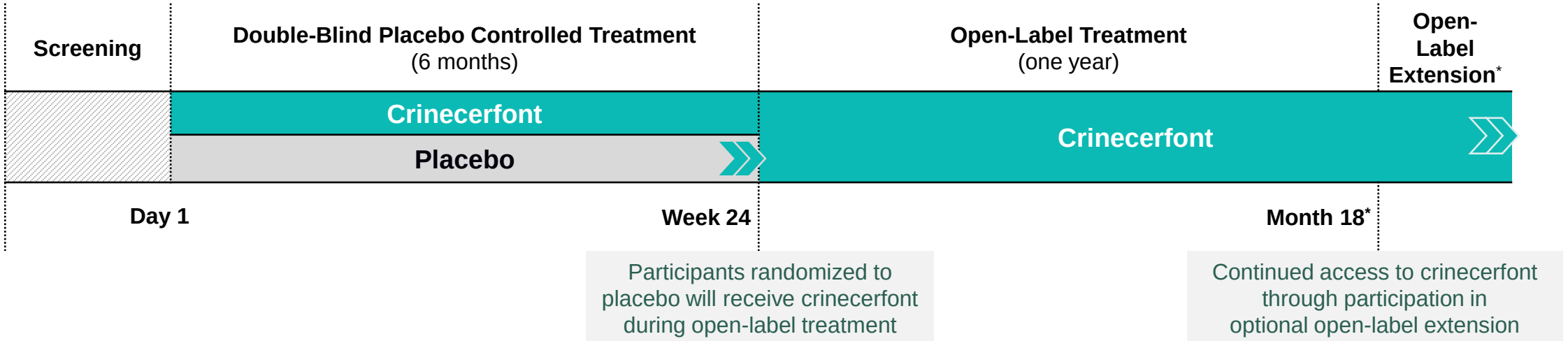
Alexandra Dubois
CAH Parent Caretaker Advocate,
CARES Foundation Board Member

Thank You for Being Here!

NEUROCRINE® BIOSCIENCES

Crinecerfont Phase 3 Study Results (Adults & Pediatrics)

CAHtalyst™ Adult Study Design



OBJECTIVE

Evaluate the efficacy, safety and tolerability of crinecerfont in adults with classic CAH

PRIMARY ENDPOINT

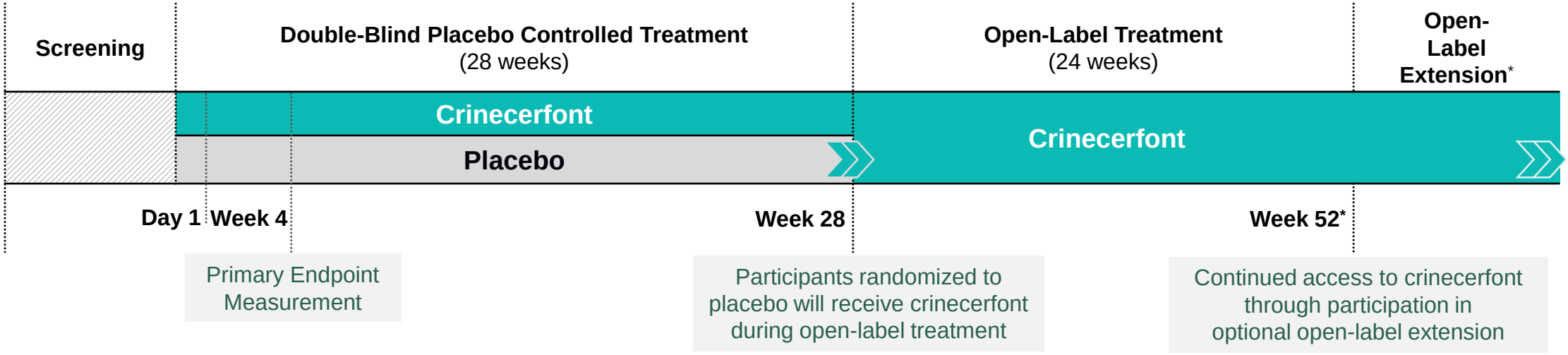
Percent change from baseline in glucocorticoid daily dose at Week 24 while maintaining androgen control

Crinecerfont is investigational and not approved in any country

NEUROCRINE BIOSCIENCES

*The duration of participation in the study is approximately 20 months for the core study and will be a variable amount of time per participant for the open-label extension

CAHtalyst™ Pediatric Study Design



OBJECTIVE

Evaluate the efficacy, safety and tolerability of crinecerfont in children and adolescents with classic CAH

PRIMARY ENDPOINT

Change from baseline in serum androstenedione at Week 4

KEY SECONDARY ENDPOINT

Percent change in glucocorticoid daily dose from baseline at Week 28 while maintaining androgen control

Crinecerfont is investigational and not approved in any country

NEUROCRINE BIOSCIENCES

*The duration of participation in the study is approximately 14 months for the core study and will be a variable amount of time per participant for the open-label extension

CAHtalyst™ Adult and Pediatric Study Design Comparisons

Similarities

Key Endpoints Focused on Androgen Reduction and Steroid Dose Reduction with Androgen Control

- Same definition of endpoints, same target dose

6-month Randomized Double-blind Placebo-Control

- First Month Steroid Stable – Evaluate Androgens
- Next ~5 Months – Active Steroid Reduction

Crinecerfont Dosing (BID, oral)

Clinical Assessments of Steroid and Androgen Impact

Differences

Ordering of Endpoints (Primary vs. Key Secondary)

Management of Steroid Reduction

- Adult Study: “Optimize on Lowest Steroid Dose”
  - “Forced” Down Titration Followed by Optimization
- Pediatric Study: “Optimize on Androgen Control”
  - Decrease Steroid Dose ONLY If Androgen Controlled

CAHtalyst™ Adult and Pediatric Study Baseline Characteristics

Study Characteristic	Adult Study (N = 182)	Pediatric Study (N = 103)	Key Takeaways
Male / Female (Proportion of Total Subjects)	51% Male 49% Female	52% Male 48% Female	Nearly Equal Male and Female
Average Age (Age Ranges)	31 Years Old (18 – 58 Years Old)	12 Years Old (4 – 17 Years Old)	Broad Age Range Representation
Average Baseline Glucocorticoid (GC) Dose*	32 mg/day (18 mg/m^2/day)	16 mg/m^2/day	Baseline GC Dose ~2x "Physiologic" (Replacement)
Average Baseline Androstenedione Level**	620 ng/dL	431 ng/dL	Poor Androgen Control (~2-3x upper end of normal) Despite High GC Dose
Body Mass Index (BMI)	47% Obese (BMI ≥ 30 kg/m^2)	58% ≥ 85th Percentile (Overweight or obese)	Highlights Metabolic Impact of Steroids, Especially Overweight at Early Age
Percent of Subjects Completing Study 24-Week (Adult) or 28-Week (Pediatric) Placebo-Controlled Treatment Period	>95%	>95%	Vast Majority Completed Placebo-controlled Period and Continuing Treatment Reflecting Trial Quality, Crinecerfont Tolerability, Unmet Need

NEUROCRINE BIOSCIENCES

* In Hydrocortisone Equivalents
** Pre-Glucocorticoid Dose

CAHtalyst™ Adult and Pediatric Study Androgen Reduction

	Percent Change in Androstenedione at Week 4 (Following Glucocorticoid Stable Period)*		
Study Characteristic	**Adult Study (N = 182)**	**Pediatric Study (N = 103)**	**Key Takeaways**
Patients Receiving Crinecerfont	-45%	-54%	Substantial and Meaningful Reduction in Androgens with Crinecerfont by 4 Weeks
Patients Receiving Placebo	+21%	+33%	Increase in Androgens on Placebo Reflecting Poor Disease Control Despite High Dose Steroids
Placebo-Adjusted Difference (Patients Receiving Crinecerfont – Patients Receiving Placebo)	-66%	-86%	Similar to Androgen Reduction Observed in Phase 2 Open-Label Studies (14 days)
P-value	<0.0001	<0.0001	

NEUROCRINE BIOSCIENCES

*Adjusted for baseline level, treatment group, stratification factors

CAHtalyst™ Adult and Pediatric Study Glucocorticoid Dose Reduction While Maintaining Androgen Control

	Percent of Subjects Achieving a Glucocorticoid Daily Dose ≤ 11 mg/m²/day While Maintaining Androgen Control		
CAHtalyst™ Trial Participants	**Adult Study @ Week 24**	**Pediatric Study @ Week 28**	**Key Takeaways**
Patients Receiving Crinecerfont	63%	30%	Substantial Percentage of Patients on Crinecerfont Achieved Physiologic GC Dose with Androgen Control
Patients Receiving Placebo	18%	0%	No Pediatric Patients on Placebo Achieved Physiologic GC Dose Reflecting Inadequacy of GC to Treat High Androgen
Placebo-Adjusted Difference (Patients Receiving Crinecerfont – Patients Receiving Placebo)	45%	30%	Similar Results in Adult and Pediatric Patients Considering Differences at Baseline and in Trials
P-value	<0.0001	0.0009*	

In Addition, Treatment with Crinecerfont in Adult and Pediatric Patients Resulted in Significant Percent Reduction in Glucocorticoid Dose while Maintaining Androgen Control (p<0.0001 both studies)

NEUROCRINE BIOSCIENCES

* p-value not adjusted for multiplicity

CAHtalyst™ Adult and Pediatric Study Safety and Tolerability

- Crinecerfont Treatment was Generally Well-Tolerated with Few Serious Adverse Events (SAEs), None Were Assessed as Related to Crinecerfont
- Most Common Adverse Events During the Double-Blind, Placebo-Controlled Period of the Adult Study were Fatigue, Headache, and Coronavirus Infection
- Most Common Adverse Events During the Double-Blind, Placebo-Controlled Period of the Pediatric Study were Headache, Fever, Vomiting, Upper Respiratory Tract Infection, and Nasopharyngitis
- No Safety Concerns Related to Adrenal Crisis

NEUROCRINE BIOSCIENCES

* p-value not adjusted for multiplicity

NEUROCRINE® BIOSCIENCES

CAH / CRINECERFONT Q&A SESSION

NEUROCRINE® BIOSCIENCES

Dr. Kevin Gorman

CHIEF EXECUTIVE OFFICER

Key Milestones in 2024 and Longer Term

2024

- **April PDUFA for Valbenazine Oral Granules Sprinkle Formulation**
- **Submitting New Drug Application for Crinecerfont in Adult and Pediatric CAH Indications**
- **Advancing Five Phase 1 Programs** including Four Muscarinic Compounds and next generation VMAT2 Inhibitor
- **Anticipating Top-Line Data for Five Phase 2 Programs**
  - Efmody for Adrenal Insufficiency and CAH in 1H
  - NBI-’845 (AMPA Potentiator) for Inadequate Response to Treatment in Major Depressive Disorder in 1H
  - NBI-’568 (M4 Agonist) for Schizophrenia in 2H
  - Luvadaxistat (DAAO Inhibitor) for Cognitive Impairment Associated with Schizophrenia in 2H
- **Developing Sustainable R&D Engine**

Longer Term

- **Anticipated Crinecerfont Approved in U.S. (2025) and in Europe (2026)**
- **Advancement of 2 Gene Therapy Programs Into Clinical Development (2025)**
- **Advancement of 20 Development Candidates (Through 2027)**
- **Sustainable R&D Engine Generating 1-2 Mid-to-Late-Stage Clinical Read-Outs Every Year**
- **Clinical Pipeline**
  - Weighted Towards Neurology vs. 2023
  - Balanced Between Biologics and Small Molecules
  - Focused on Clinically and / or Genetically Validated Targets
  - Majority of Candidates Considered “Next” or “Best-In-Class”
- **INGREZZA® (valbenazine) Market Exclusivity Into 2038**

Building a Leading Neuroscience-Focused Company

NEUROCRINE® BIOSCIENCES

OPEN Q&A SESSION

NEUROCRINE® BIOSCIENCES

THANK YOU!

NEUROCRINE® BIOSCIENCES

Neurocrine Biosciences 2023 Analyst Day

December 5, 2023