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Focused on developing and commercializing novel therapies for rare endocrine disorders with significant unmet medical need

Corporate Presentation

JANUARY 2021

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This presentation discusses a product candidate that is under clinical study and which has not yet been approved for marketing by the U.S. Food and Drug Administration. No representation is made as to the safety or effectiveness of this product candidate for the use for which it is being studied.

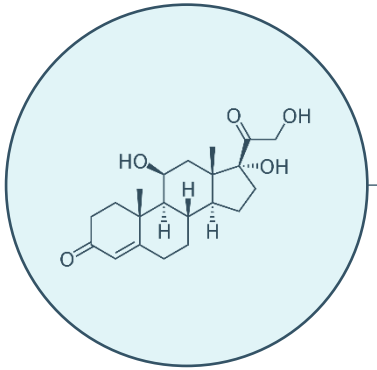
SPRUCE AT-A-GLANCE

Tildacerfont poised to transform treatment paradigm in classic CAH	**Two late-stage clinical studies initiated; Data expected by 1H 2022. Studies designed to support registration in U.S. and Europe in 2023**
Multiple expansion opportunities	**Initiation of Phase 2 programs in pediatric classic CAH and a rare form of polycystic ovary syndrome (PCOS) in 2H 2021**
Significant commercial opportunity	**$3B+ worldwide market opportunity in classic CAH**
Strong IP protection	**Comprehensive IP portfolio based on issued patents provides exclusivity to 2038 in U.S. combined with Orphan Drug Designation in U.S. and Europe**
Highly experienced leadership team	**Management has contributed to development and commercial launch of 40 products, including within endocrine and rare disease space**

Classic CAH Overview

CLASSIC CAH DISEASE OVERVIEW

Classic CAH is a chronic and potentially life-threatening rare disease



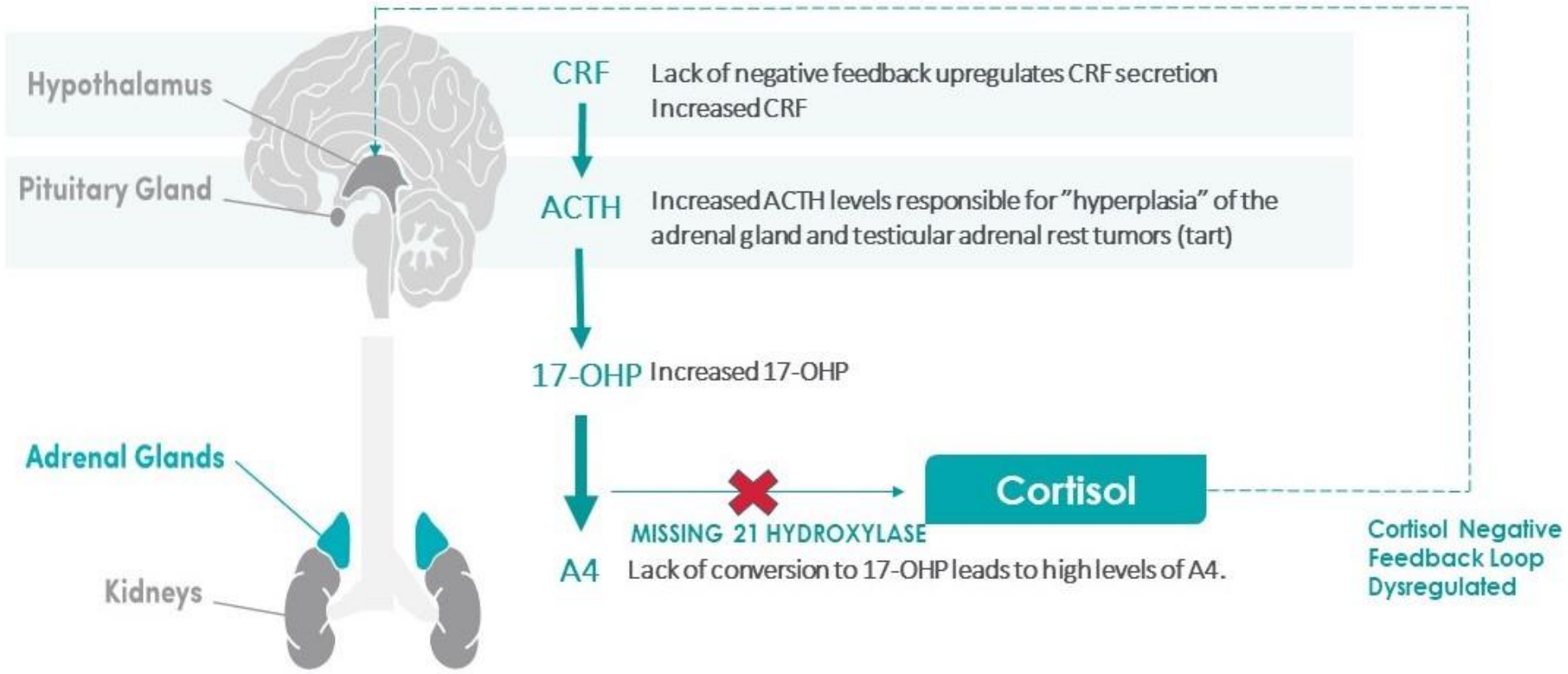
Classic CAH is an autosomal recessive disease characterized by an inability to produce cortisol, leading to a chronic imbalance of key hormones and an overproduction of adrenal androgens.

Due to the severity and high incidence of the disease, most developed countries have established newborn screening programs to test for classic CAH at birth.

We estimate the total classic CAH population to be approximately 20,000-30,000 people in the U.S. and 50,000 people in the EU.

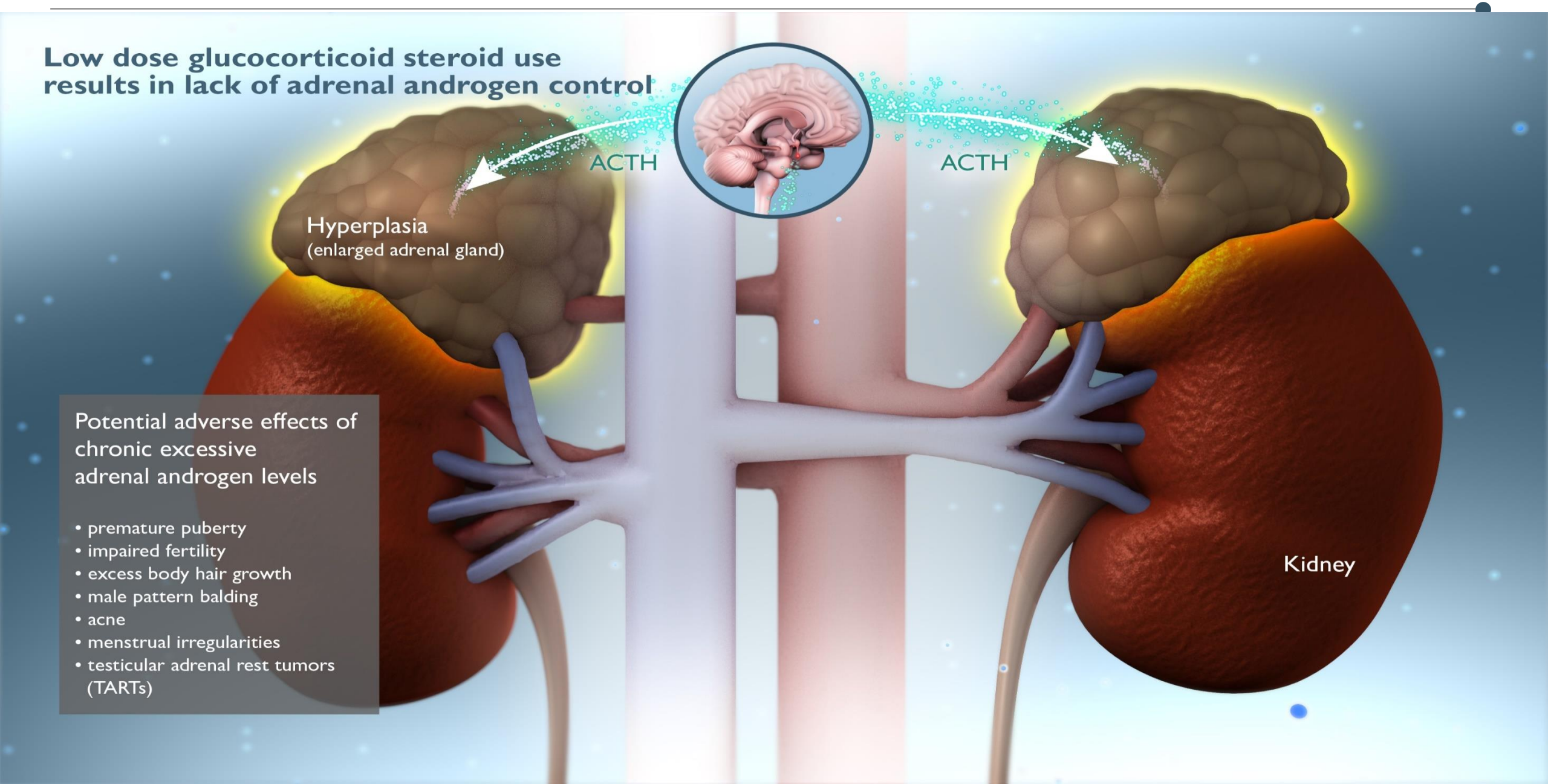
HPA AXIS FUNCTION IN CLASSIC CAH PATIENTS

Lack of cortisol leads to overproduction of ACTH and precursor steroid molecules, resulting in excessive adrenal androgens

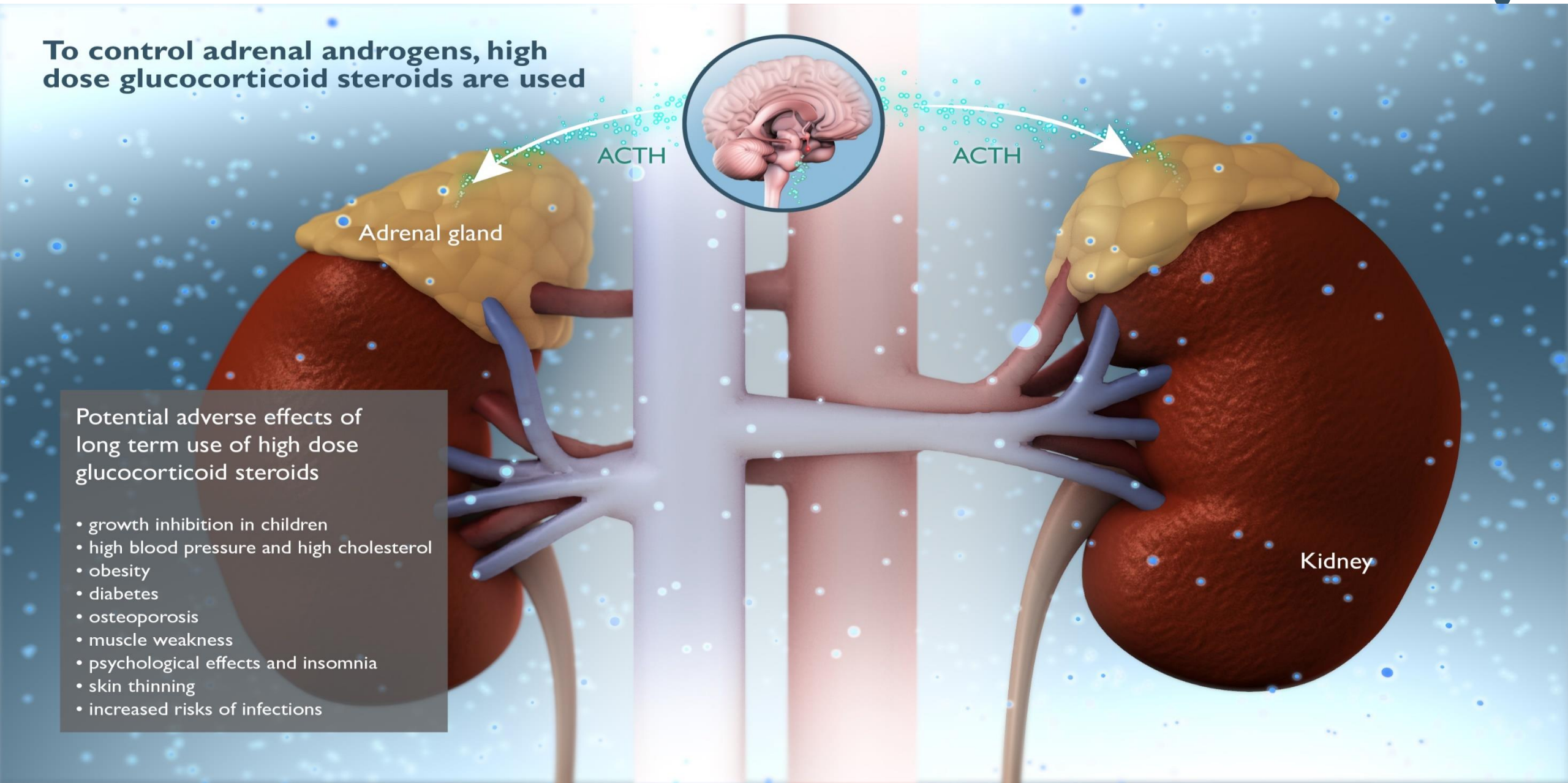


The dysregulation of the HPA axis in classic CAH.

LOW DOSE GLUCOCORTICOID USE RESULTS IN LACK OF ANDROGEN CONTROL



HIGH DOSE GLUCOCORTICOIDS ARE USED TO CONTROL ANDROGENS



Tildacerfont
Clinical Development Program

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ABOUT TILDACERFONT

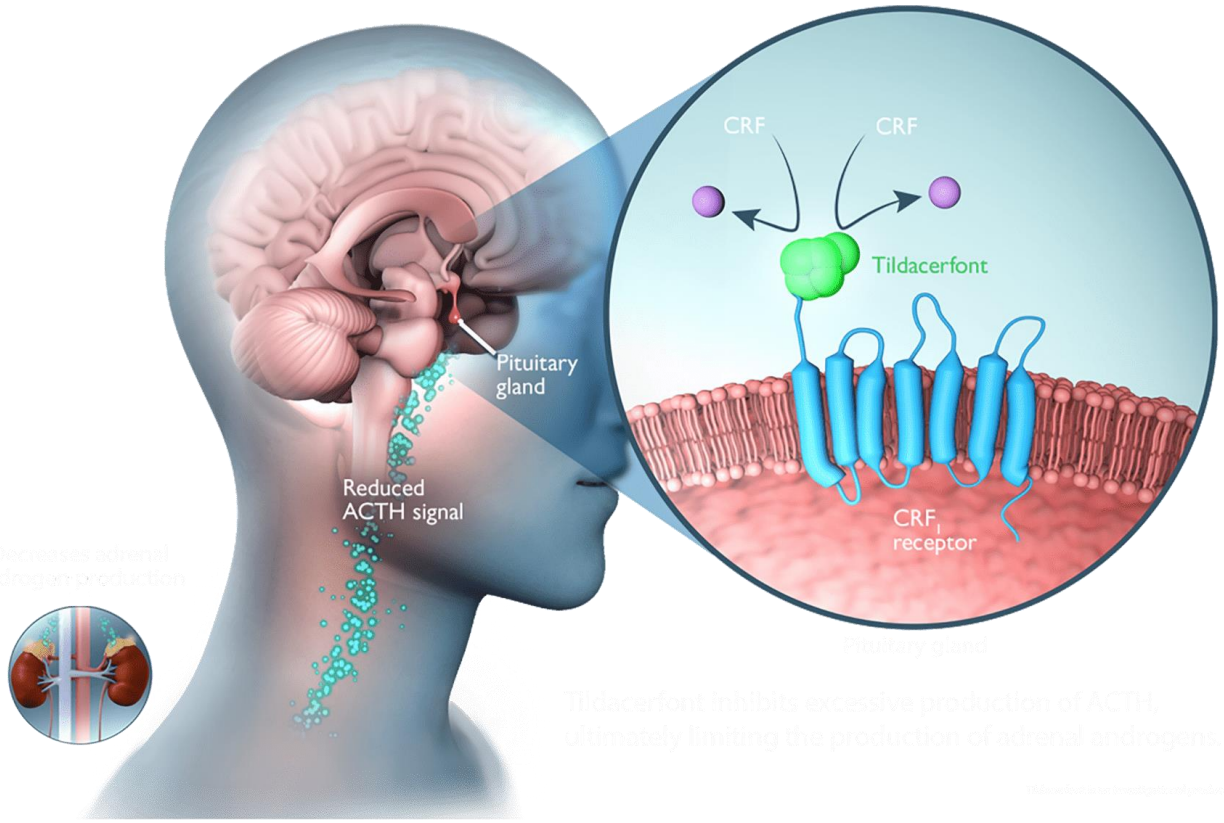
Spruce aims to **transform the treatment paradigm** and **offer markedly improved disease control** and **reduced steroid burden** with a well-tolerated, non-steroid approach to classic CAH

Tildacerfont may eliminate the choice between excessive adrenal androgens and GC use

MOA

Tildacerfont inhibits secretion of ACTH from the pituitary gland

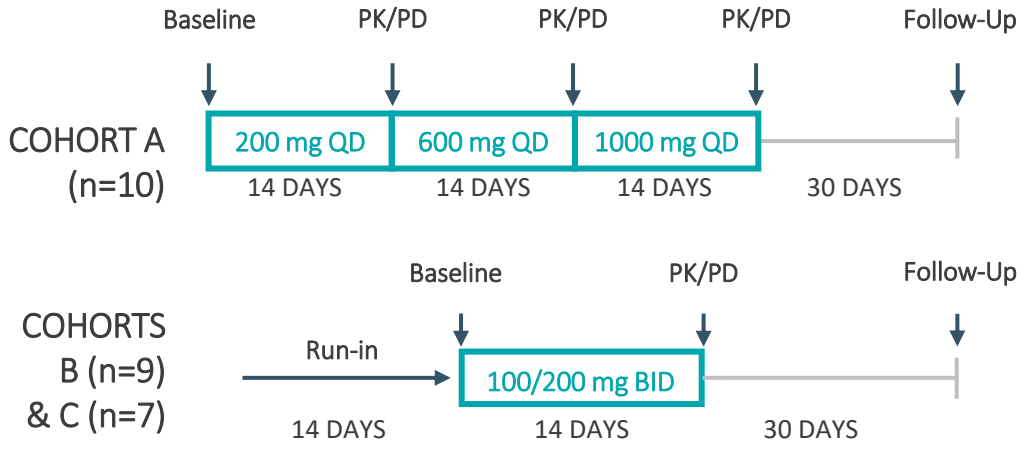
Tildacerfont blocks CRF1 receptors at the anterior pituitary gland to decrease secretion of ACTH, hormones, such as 17-OHP, and androgens, such as A4.



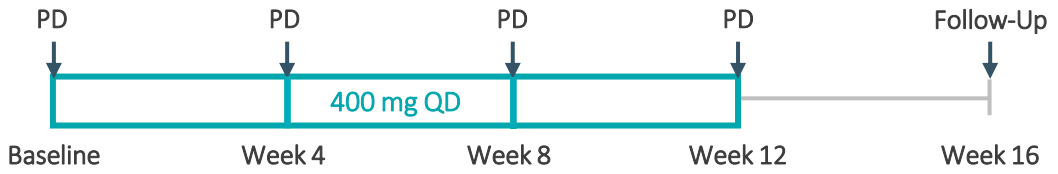
COMPLETED TILDACERFONT TRIALS

Tildacerfont was generally well-tolerated in seven clinical trials exposing 171 subjects with no drug-related SAEs

SPR001-201 – Clinical Proof of Concept



SPR001-202 – 12-week, open label, n=11



- Entry criteria: Adult>18 yrs w/ classic CAH
- 17-OHP ≥800 ng/dL (~4X ULN)
- Stable GC doses

TOP LINE STUDY TAKEAWAYS

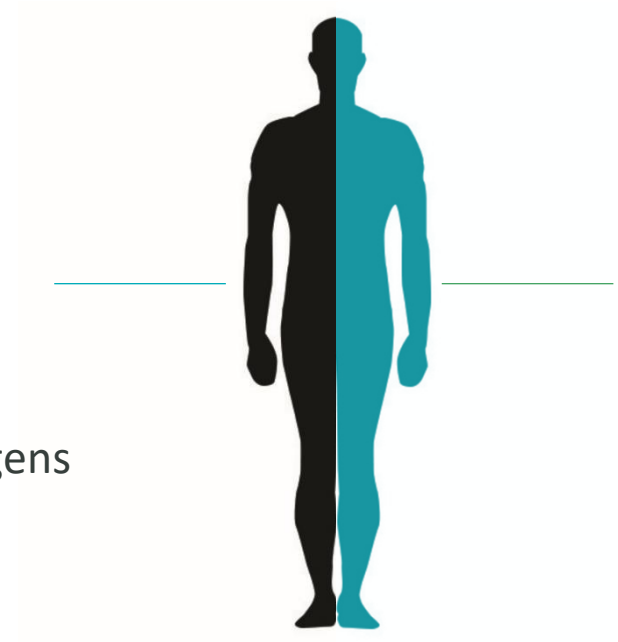
- Observed reductions in adrenal androgens at 2 weeks (Study 201) and 3 months (Study 202)
- Demonstrated robust reduction in ACTH at lowest dose studied (200mg TDD)
- Identified two distinct patient populations with either *poor disease control* or *good disease control*

TWO DISTINCT PATIENT GROUPS IDENTIFIED

Patient groups reinforce the **difficult choice** between **excessive adrenal androgens and high GC dosing**

POOR DISEASE CONTROL

- Highly elevated adrenal androgens
- Lower GC dosing < 30mg/day hydrocortisone equivalent (HCe)
- Unmet need to reduce adrenal androgens and improve related clinical outcomes



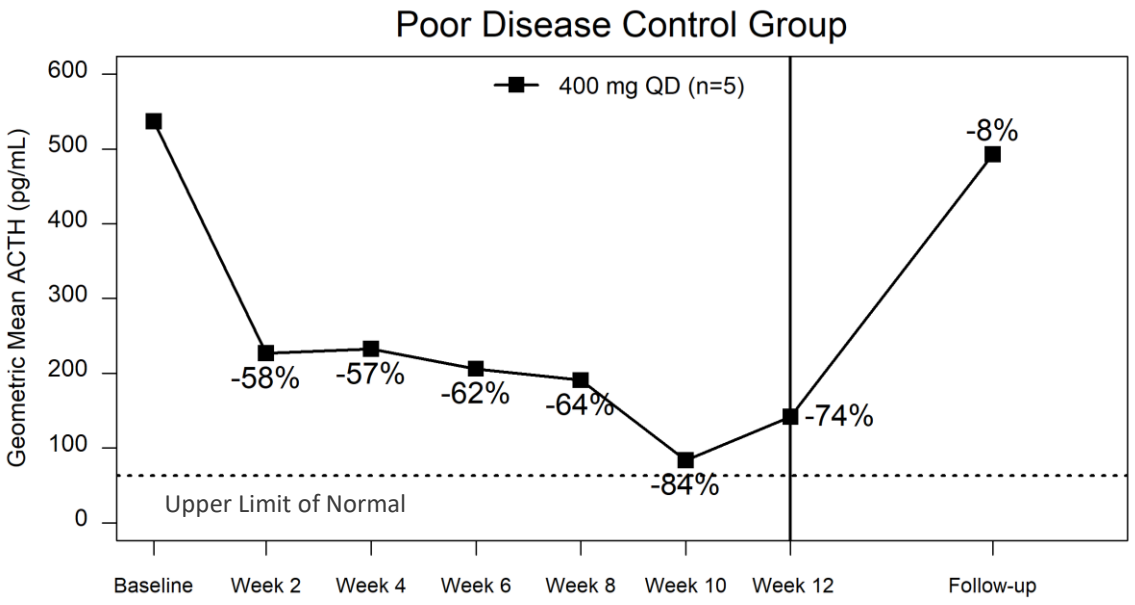
GOOD DISEASE CONTROL

- Normal or near normal adrenal androgens
- Higher GC dosing > 30mg/day hydrocortisone equivalent (HCe)
- Unmet need to reduce GC dose and improve related clinical outcomes

TILDACERFONT STUDY 202 – ACTH

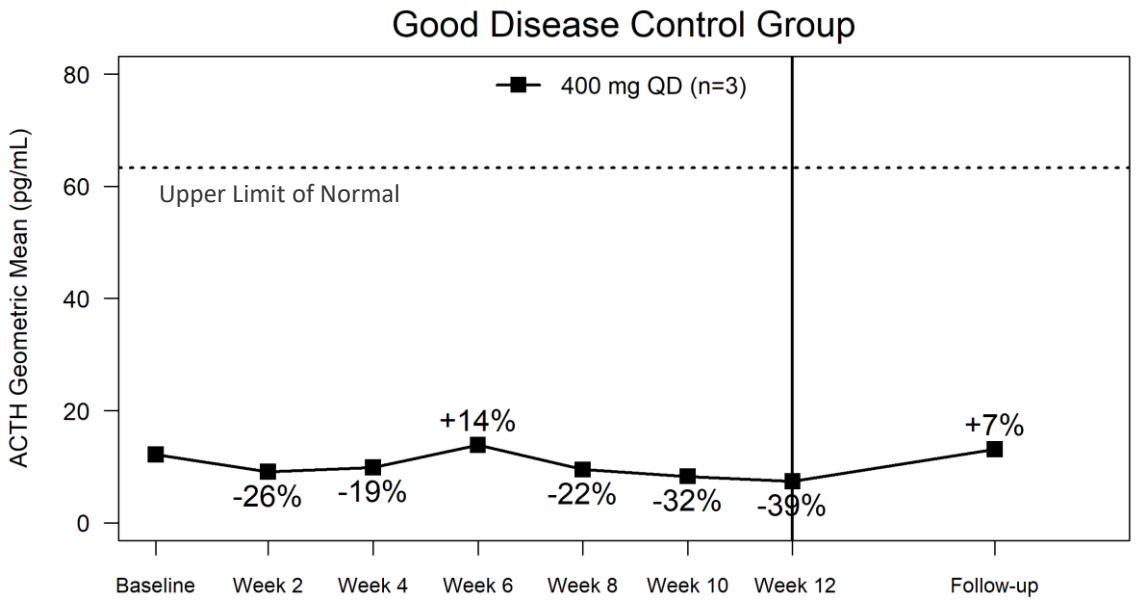
- In poor disease control group, demonstrated robust initial drop in ACTH at week 2, followed by further reduction over 12 weeks
- Maximum reduction in ACTH in poor disease control group of 84% at week 10 of study

POOR DISEASE CONTROL (<30mg HCe)



- Normalization of ACTH in 60% of patients achieved [1]

GOOD DISEASE CONTROL (>30mg HCe)



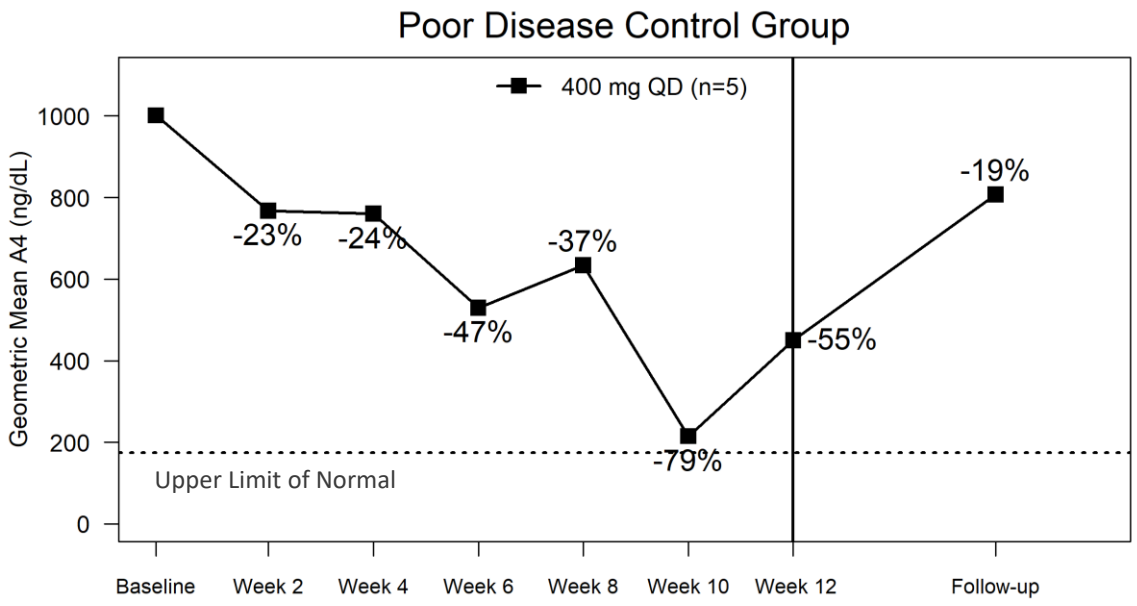
- No excessive suppression of adrenal function

[1] One subject at week 2 prior to discontinuation from the trial and two subjects during month 3

TILDACERFONT STUDY 202 – A4

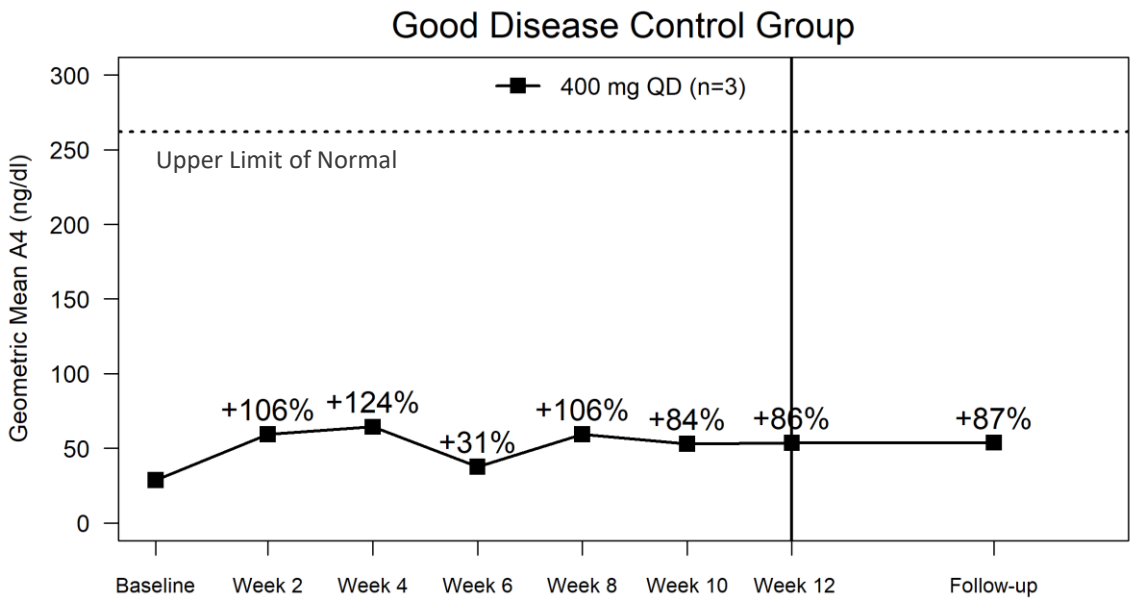
- In poor disease control group, demonstrated initial drop in A4 at week 2, followed by further reduction over 12 weeks
- Maximum reduction in A4 in poor disease control group of 79% at week 10 of study

POOR DISEASE CONTROL (<30mg HCe)



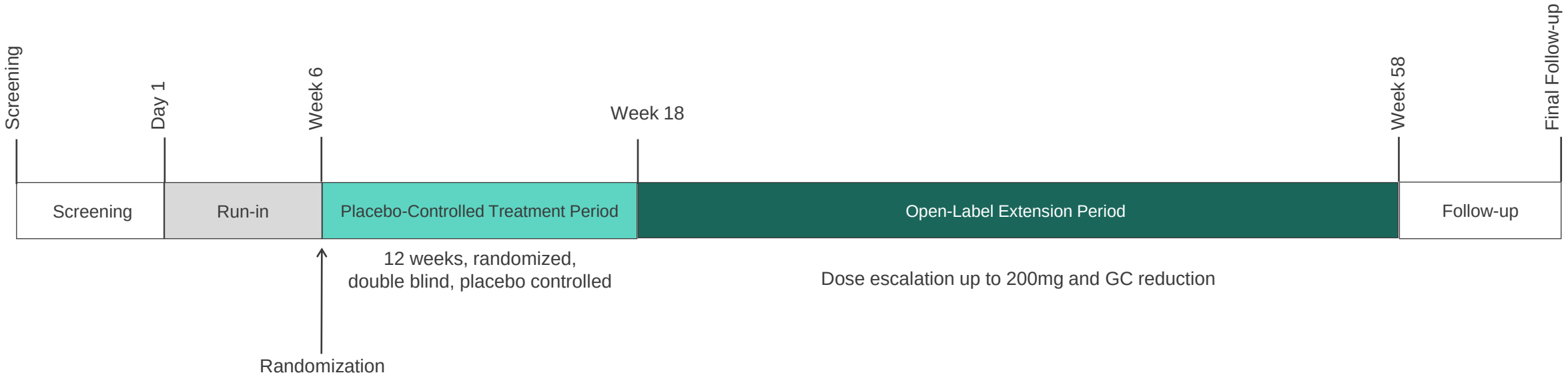
- Normalization of A4 in 40% of patients achieved

GOOD DISEASE CONTROL (>30mg HCe)



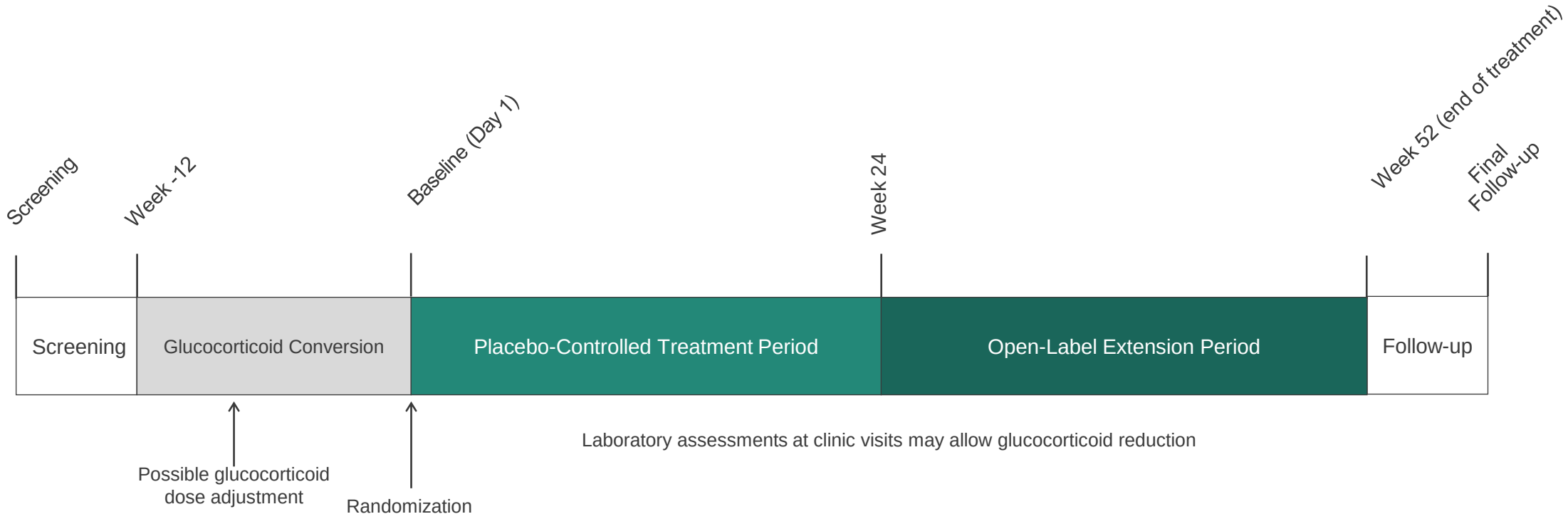
- No excessive suppression of adrenal function

ADRENAL ANDROGEN REDUCTION STUDY (CAHmelia-203)



Design	Randomized, Double Blind, Placebo-controlled dose-ranging study x 12 weeks + 40 week open label extension
Sample size & Dose	72 patients; Tildacerfont 50, 100, or 200 mg QD vs placebo
Key Eligibility Criteria	Adults ≥18 yrs, Classic CAH and poor disease control, on stable GC regimen ≥ 15mg/day
Endpoints	1º Endpoint: Change in androstenedione (A4) from Randomization baseline to Week 18 Additional Endpoints: Change in androgens/hormones, TARTs in men, clinical CAH symptoms, GC dose

GC REDUCTION STUDY (CAHmelia-204)



Design	**Randomized, Double Blind, Placebo-controlled GC-sparing study x 24 weeks plus 28 weeks open-label extension**
Sample Size & Dose	60 patients; Tildacerfont 200 mg QD vs placebo
Key Eligibility Criteria	Adults ≥ 18 yrs with classic CAH & good disease control, on stable GC regimen ≥ 30 mg/day
Endpoints	1º Endpoint: Change in GC dose from Randomization Baseline at Week 24 Additional Endpoints: Change in Metabolic parameters, blood pressure, weight, bone turnover, body composition, bone mineral density

PEDIATRIC CLASSIC CAH

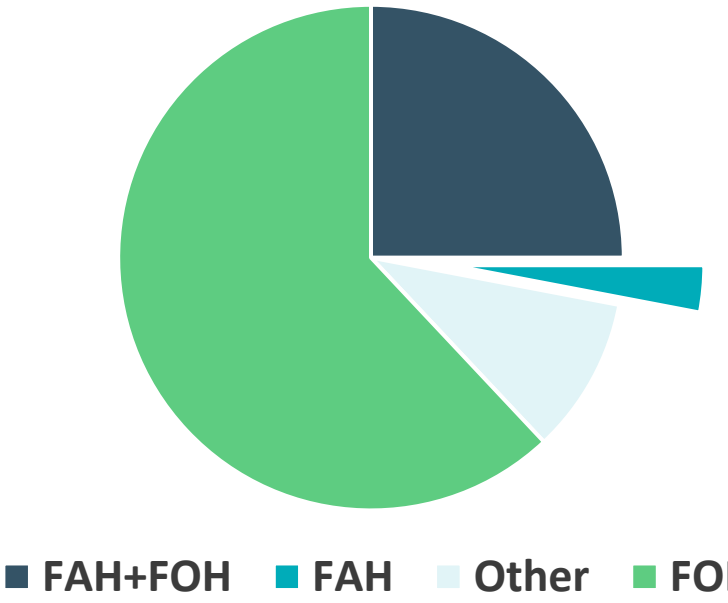
Imbalance between androgen excess and GCs lead to irreversible impacts on childhood development

- Autosomal recessive disease screened for and diagnosed at birth
- Urgent need for androgen-lowering and glucocorticoid-reduction therapy
- Effects of disease can include premature puberty, as young as 5 years old due to both elevated androgens and GC therapy
- High doses of glucocorticoids can prevent a child from growing to their full height
- **FDA and EMA feedback received for Phase 2 program, anticipated to initiate in 2H 2021**

TILDACERFONT IN POLYCYSTIC OVARY SYNDROME (PCOS)

Tildacerfont may offer a therapeutic option for a subpopulation of women with PCOS by lowering ACTH levels and reducing adrenal androgen levels

PCOS by androgen source



FAH = Functional Adrenal Hyperandrogenism; FOH = Functional Ovarian Hyperandrogenism; Other = Iatrogenic and Obesity

- Women with FAH PCOS have a hyperresponsivity to ACTH
- This drives elevated androgen levels, and PCOS symptoms
- Tildacerfont, by reducing ACTH and A4, may reduce symptoms associated with PCOS FAH
- FAH PCOS can be easily diagnosed via current tests
- FAH PCOS represents 150-200,000 women in US

INITIATION OF PHASE 2 PROOF-OF-CONCEPT TRIAL PLANNED IN 2H 2021*

Commercial Opportunity and Milestones

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COMMERCIAL OPPORTUNITY – CLASSIC CAH

- Large rare disease, up to 80,000 patients in U.S./EU
- $3B+ global market opportunity[1]
- Orphan drug pricing anticipated
- IP: Composition of Matter (2027)[2] / Methods (2038)
- Orphan Drug Designation: U.S. (7.5 years) / EU (12 years)[3]

1. Based on industry reports
2. Absent any patent term adjustments or extensions
3. Assumes 6-month (U.S.) and 2-year (EU) extension if clinical trials are conducted in accordance with agreed-upon pediatric investigational plan

KEY ANTICIPATED MILESTONES

1H2021	File IND in women with PCOS due to functional adrenal hyperandrogenism
2H2021	Initiate Phase 2 proof-of-concept trial in PCOS*
2H2021	Initiate Phase 2 trial in pediatric classic CAH
1Q22	Topline results in adult classic CAH (CAHmelia-203)
1H2022	Topline results in adult classic CAH (CAHmelia-204)

*Subject to clearance of IND

INVESTMENT HIGHLIGHTS

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