# Atypical Body Composition in Individuals with Prader-Willi Syndrome

Prader-Willi syndrome (PWS) is a rare genetic disorder (~1 in 15,000 births) and the most common genetic cause of syndromic obesity<sup>1,2</sup>

- Individuals with PWS have an intrinsic atypical body composition characterized by increased fat mass and reduced lean body mass (LBM), evident from infancy and persisting into adulthood, even among those with normal BMI<sup>1,3-5</sup>
- Hyperphagia, as well as obesity, are among the clinical conditions of PWS that may typically develop in childhood and, if present, can each further impact body composition.<sup>3,4,6-8</sup>
- Not all individuals with PWS are obese; excessive weight or obesity affects ~40% of children/adolescents and ~80-90% of adults.<sup>3,8</sup> However, in PWS individuals who are obese, PWS body composition remains distinct from non-syndromic obesity: compared to BMI-matched obese individuals, PWS is characterized by elevated total and subcutaneous fat mass, reduced LBM, and lower resting energy expenditure.<sup>2-4,8,9</sup>

# **Etiology of PWS**

PWS results from loss of paternally expressed genes on chromosome 15q11.2-q13.<sup>2,3</sup>

# Phenotypes of Individuals with PWS\*

# Children with PWS

"Pear shaped" or endomorphic compared with BMImatched individuals with obesity, fat mass is predominately subcutaneous and concentrated in the trunk and proximal limbs<sup>3,4,9</sup>

Short stature<sup>6</sup>

Even with normal BMI, there is markedly reduced **LBM** (particularly in limbs) and higher fat mass<sup>1,4</sup>

Small hands and feet 1,6

Infants with PWS, even when underweight, exhibit elevated body fat1

# Adolescents & Adults with PWS

Lack of normal pubertal growth results in reduced or short adult stature1

Relative to BMI-matched obese cohorts, there is greater proportion of subcutaneous fat, less visceral fat accumulation. and a lower trunk-toappendicular fat mass

Compared with BMImatched individuals with non-syndromic obesity, markedly higher fat mass and very low LBM<sup>3,9</sup>

Characteristic reduction in **LBM** is associated with reduced resting energy expenditure and notable poor motor function of the lower limbs, and reduced exercise capacity<sup>3,5</sup>

\*Conceptual schematic informed by recent PWS publications; illustrative only and not based on Soleno data

# **Key Body Composition Parameters in PWS**

Anthropometric indicators like weight or BMI provide limited insights into body composition in PWS, particularly in children and adolescents whose growth patterns differ. <sup>4,7</sup> Additional parameters offer a more accurate clinical view of the body-composition patterns across developmental stages and qualitative shifts in PWS.

## Weiaht



Measures total body mass, not quality of tissue4



May appear 'normal' despite excess fat and low muscle mass<sup>4</sup>

## **BMI Z-score**



Age/sex-standardized BMI- useful for tracking trajectories in pediatrics, relative to peer cohort

## Lean body mass



LBM = total body weight minus fat mass; (muscle, bone, water, organs)

## Fat mass



Total adipose tissue = total body weight minus LBM

# Lean mass index



Lean tissue metric that adjusts for stature: LMI = LBM ÷ height

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