BACKGROUND: 22q11.2 DELETION SYNDROME

- 22q11.2 deletion syndrome (22q) is the second most common chromosomal disorder after Down syndrome.
- 22q occurs in 1 in 3000 to 1 in 6000 live births.
- The deletion of genes such as Tbx1 may be responsible for characteristic signs (such as heart defects, a cleft palate, distinctive facial features, hearing loss, and low calcium levels) and behavioral problems.
- Children with 22q are at increased risk for several psychiatric disorders, including anxiety, social withdrawal, attention-deficit hyperactivity disorder (ADHD), cognitive impairment, autism spectrum disorder (ASD), and mood disorders, as well as psychotic disorders and schizophrenia.
- Approximately 40% of these children suffer from some type of anxiety disorder.
- Specific phobias are most common, followed by generalized anxiety disorder, separation anxiety, and obsessive-compulsive disorder.
- Early negative experience has been shown to increase the risk of anxiety and is associated with atypical development of the physiological stress response.
- Serious medical complications, such as congenital heart disease, feeding difficulties, and multiple surgeries or hospitalizations, may also predispose some children to anxiety disorders due to stressors associated with repeated medical procedures or poor sense of control over one’s body.
- The presence of anxiety symptoms in children with 22q is negatively correlated with adaptive function and impacts everyday living skills.

BACKGROUND: CANNABIDIOL AND ZYN002

- Disruption in the endocannabinoid system (ECS) is one of the proposed mechanisms underlying symptoms affecting children with neurodevelopmental disorders.
- Cannabidiol acts as a negative allosteric modulator at presynaptic type 1 cannabinoid receptors.
- Cannabidiol has also shown activity at serotonin 5HT1A, gamma-aminobutyric acid A, and dopamine D2 and D3 receptors.
- ZYN002 is a pharmaceutically produced (not plant-derived) cannabinoid transdermal gel in clinical development for the treatment of behavioral symptoms associated with 22q, Fragile X syndrome (FXS), and ASD.
- ZYN002 does not contain delta-9-tetrahydrocannabinol (THC) and avoids conversion to THC in the stomach due to transdermal application.

WHY STUDY ZYN002 IN 22q?

- Anxiety and a constellation of behavioral symptoms are similar between 22q, FXS, and ASD.
- ZYN002 has been shown to have potential benefit in FXS and ASD.
- Dysfunction in the ECS may be present in all 3 disorders.
- ZYN002 does not contain THC, THC may increase the risk for schizophrenia, and THC-containing cannabinoids should be avoided in individuals with 22q since they are at increased risk of psychosis.