PTC Therapeutics and Invitae have partnered to provide no-cost genetic testing, genetic counseling, and family screening programs for individuals with a suspected neurotransmitter disorder, such as Aromatic L-amino Acid Decarboxylase (AADC) deficiency or cerebral palsy (CP) spectrum disorder of unknown etiology.
AADC deficiency is a genetic disease associated with defects in neurotransmitter synthesis that can lead to a manifestation of a broad spectrum of symptoms.\(^1,2\)

The most common symptoms of this autosomal recessive disease are\(^1,4\):

- Hypotonia
- Developmental delay
- Movement disorders, especially oculogyric crises

In AADC deficiency, mutations in the dopa decarboxylase (DDC) gene result in reduced AADC enzyme activity, leading to severe combined deficiency of dopamine, serotonin, norepinephrine, and epinephrine.\(^1,2,5,6\)

Symptoms of neurotransmitter disorders can overlap with those of other neurological disorders, which can make diagnosis challenging.\(^7\)

Many of the most common symptoms of AADC deficiency can also be attributed to a number of other conditions such as cerebral palsy and epilepsy, resulting in potential misdiagnosis.\(^1,2,8-11\)
Accurate identification of AADC deficiency can help improve the care and management of patients\textsuperscript{5,12}

AADC deficiency may be misdiagnosed or go undiagnosed, delaying treatment and proper management\textsuperscript{1,2,12}

Despite symptom onset during infancy, diagnosis is typically delayed\textsuperscript{1}:
- The mean age of diagnosis is \textbf{3.5 years}
- The age range of diagnosis is \textbf{2 months to 23 years}

One or a combination of red-flag diagnostic clues should prompt testing for a neurotransmitter disorder, like AADC deficiency:

- Oculogyric crises\textsuperscript{2,12,13}
- Autonomic symptoms\textsuperscript{12}
- Normal EEG and neuroimaging\textsuperscript{1,9,10,12}
- Diurnal variation\textsuperscript{1,8,14}

EEG=electroencephalogram.
Because prompt diagnosis can help improve the care and management of patients with AADC deficiency and other neurotransmitter disorders, PTC Pinpoint is a no-cost program offering genetic testing and counseling and family screening for individuals suspected of having a neurotransmitter disorder, such as AADC deficiency, in the US and Canada.\textsuperscript{5,12}

**Designed to help you support your patients and their families with genetic insights**

Not knowing the underlying cause of a child’s signs and symptoms can be difficult for families. PTC Therapeutics and Invitae have come together with the PTC Pinpoint testing program to provide information to healthcare providers that can aid in a differential diagnosis. The PTC Pinpoint testing program is designed to help families by offering:

- No-cost testing programs for:
  - Neurotransmitter disorders
  - CP spectrum disorders
- Genetic counseling post testing
- Family follow-up testing for relatives of those with confirmed or likely pathogenic variants

The goal of this program is to test for information about genetic variants that can hasten a diagnosis and give insight into the appropriate course of action for families and their children.

For more information or to order a test, please visit: [invitae.com/en/PTC-Pinpoint-CP-Spectrum](http://invitae.com/en/PTC-Pinpoint-CP-Spectrum).
The CP Spectrum program breaks down many barriers to genetic testing for CP. Through PTC Pinpoint™, individuals with symptoms suggestive of CP without evidence for acquired brain injury have access to no-charge genetic testing and counseling.

The program analyzes 265 genes and may help identify an underlying etiology, such as AADC deficiency, which may be amenable to specific medical management or treatment options.

**Signs and symptoms that are suggestive of an underlying genetic etiology for CP include**\(^{10,14}\):  
- No documented perinatal risk for brain injury  
- Full-term birth  
- Brain MRI that is normal or inconsistent with acquired brain injury  
- Onset of abnormal motor symptoms after a period of normal development  
- Progressive neurologic symptoms  
- Fluctuation of muscle tone or motor symptoms  
- Worsening of neurologic symptoms with fever and/or illness  
- Hypotonia as an isolated symptom  
- Ataxia as a prominent feature  
- Evidence of peripheral neuromuscular disease  
- Abnormal eye movements  
- Family history of similarly affected individuals

**Program eligibility**  
This program is available to patients in the US and Canada with symptoms suggestive of cerebral palsy in the absence of risk factors for an acquired brain injury.

For more information or to order a test, please visit: [invitae.com/en/PTC-Pinpoint-CP-Spectrum](http://invitae.com/en/PTC-Pinpoint-CP-Spectrum).
The PTC Pinpoint™ program offers testing with the Invitae Neurotransmitter Disorders program, which analyzes up to 27 genes that are associated with disorders of monoamine metabolism, GABA metabolism, and neurotransmitter receptors and transporters.

Neurotransmitter disorders lead to a range of neurological manifestations in childhood, including:

- Developmental delay
- Motor disorders
- Epilepsy
- Autonomic dysfunction
- Neuropsychiatric features

Biochemical diagnosis of neurotransmitter disorders often requires extraction of cerebrospinal fluid. In such cases, molecular testing may help avoid a lumbar puncture and the associated risks for the patient.

Program eligibility
This program is available to patients in the US and Canada who are suspected of having, or have clinical symptoms consistent with, a neurotransmitter disorder.

For more information or to order a test, please visit: [invitae.com/en/PTC-pinpoint](http://invitae.com/en/PTC-pinpoint).

GABA=gamma-aminobutyric acid.
To order a test for your patients, here’s what to expect:

**Place your order online***

- Under Test Selection, click the Partnership Programs tab and enter the appropriate Partner Code
  - Neurotransmitter Disorder program: **PTC**
  - CP Spectrum program: **CPSD**
- Use the search bar to find and select the appropriate program
  - Invitae Neurotransmitter Disorders
  - Invitae Cerebral Palsy Spectrum Disorders
- Fill in the required patient information
- Under Billing Information, select Institutional Billing and leave all fields blank
- Complete the Order Authorization section and submit the order

*You can also download a paper order form on the website.

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**Collect a sample**

- Order a specimen **collection kit**
- Collect the specimen and ship it back to Invitae
- Include the signed **eligibility criteria form** with the specimen

For additional information, please see **specimen and shipping requirements**.

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**Results**

- Once Invitae receives the sample, you will receive the results in 10-21 calendar days, on average
- If you created an online account, you can view the status of your order by logging in to your account
- You will receive a notification email once the test results are ready
Genetic counseling through PTC Pinpoint

Support for understanding and navigating genetic testing is the best way to empower families to make informed decisions about their children’s and their own health and care. As an additional resource to offer your patients, individuals tested through the PTC Pinpoint program are eligible for post test genetic counseling to help them understand their test results. This service is provided through GeneMatters™, a third-party genetic counseling service, and is made available by Invitae at no charge as part of the program.

To schedule a genetic counseling appointment, please contact GeneMatters at 1-866-741-5331 or schedule online at: gene-matters.com.

Family follow-up testing

Invitae offers family variant testing for all blood relatives of patients who undergo testing at Invitae and are found to have a pathogenic or likely pathogenic variant.

Our family variant testing reports on the variant(s) that are identified in the original family member, as well as any other pathogenic variant(s) found in the full gene.

If a patient is found to have a pathogenic variant through the PTC Pinpoint program, all their blood relatives are eligible for family variant testing.

To test a family member through PTC Pinpoint, please fill out a PTC Pinpoint order form.

For more information about family screening, please visit: invitae.com/family.
PTC Therapeutics and Invitae have partnered to bring you and your patients PTC Pinpoint at no cost, which offers:

- Genetic testing for those suspected of having a neurotransmitter disorder, such as AADC deficiency, or a CP spectrum disorder of unknown etiology
- Genetic counseling
- Family screening

For more information or to order a test, please visit: invitae.com/en/PTC-Pinpoint-CP-Spectrum.


About PTC Therapeutics
PTC is a science-driven, global biopharmaceutical company focused on the discovery, development, and commercialization of clinically differentiated medicines that provide benefits to patients with rare disorders. PTC’s ability to globally commercialize products is the foundation that drives investment in a robust and diversified pipeline of transformative medicines and our mission to provide access to best-in-class treatments for patients who have an unmet medical need.

About Invitae
Invitae Corporation is a leading medical genetics company, whose mission is to bring comprehensive genetic information into mainstream medicine to improve healthcare for billions of people. Invitae’s goal is to aggregate the world’s genetic tests into a single service with higher quality, faster turnaround time, and lower prices.

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