UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT

Pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934

Date of report (date of earliest event reported): July 11, 2022

TONIX PHARMACEUTICALS HOLDING CORP.

(Exact name of registrant as specified in its charter)

Nevada	**001-36019**	**26-1434750**
(State or Other Jurisdiction of Incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**

26 Main Street, Chatham, New Jersey 07928
(Address of principal executive offices) (Zip Code)

Registrant's telephone number, including area code: (862) 904-8182

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (see General Instruction A.2. below):

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock	TNXP	The NASDAQ Capital Market

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§ 230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§ 240.12b-2 of this chapter).

Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 7.01 Regulation FD Disclosure.

On July 11, 2022, the Company presented certain information regarding the Company and its product candidates at the World Orphan Drug Congress USA 2022 (the "Presentation"). The Presentation, which may contain nonpublic information, is filed as Exhibit 99.01 hereto and incorporated herein by reference.

The information in this Item 7.01 of this Current Report on Form 8-K, including Exhibit 99.01 hereto, shall not be deemed "filed" for purposes of Section 18 of the United States Securities Exchange Act of 1934 (the "Exchange Act") or otherwise subject to the liabilities of that section, nor shall they be deemed incorporated by reference in any filing under the United States Securities Act of 1933 or the Exchange Act, except as shall be expressly set forth by specific reference in such a filing.

Item 9.01 Financial Statements and Exhibits.

(d)

Exhibit No.	**Description.**
99.01	Presentation by the Company
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

SIGNATURE

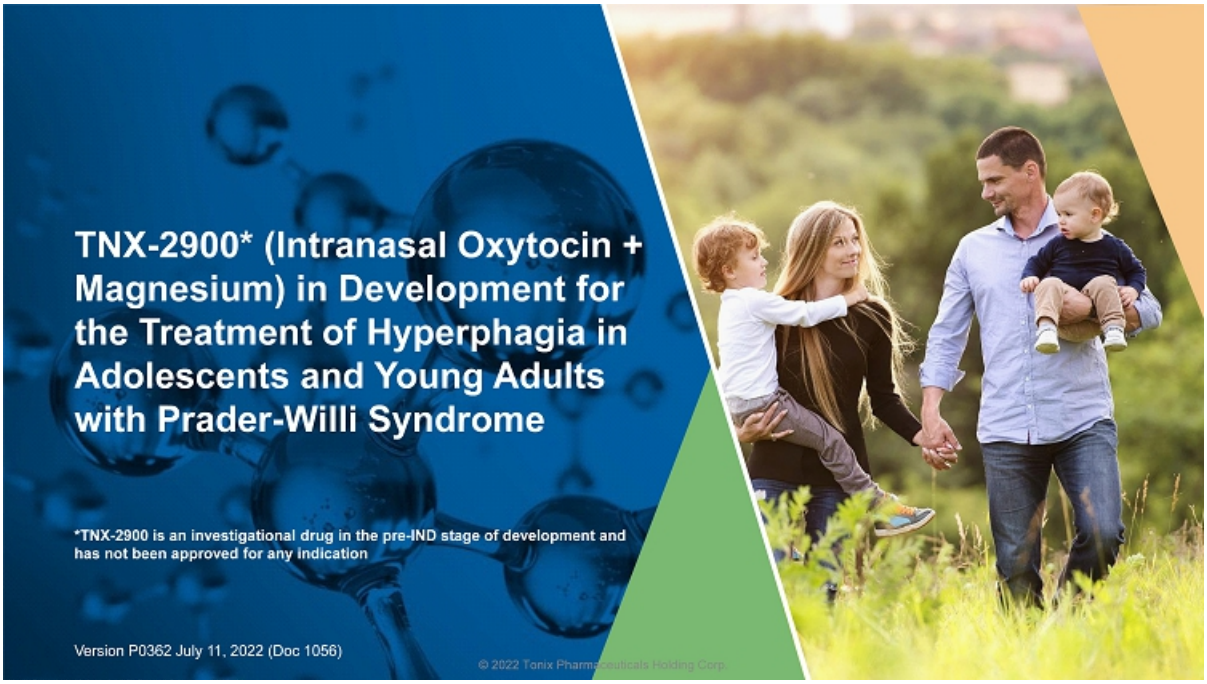
Pursuant to the requirement of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned thereunto duly authorized.

TONIX PHARMACEUTICALS HOLDING CORP.

Date: July 12, 2022

By: /s/ Bradley Saenger
Bradley Saenger
Chief Financial Officer

Exhibit 99.01



TNX-2900*: Prader-Willi Syndrome
Intranasal Potentiated Oxytocin (OT) with Magnesium

RARE DISEASE PORTFOLIO

PROFILE

Prader-Willi Syndrome is the most common genetic cause of life-threatening childhood obesity

- Rare disease occurring in 1 in 10,000 to 1 in 30,000 births

Symptoms include lack of suckling as infants, poor muscle strength, and constant hunger (hyperphagia) in adolescents and young adults

- In animal models, OT has improved suckling and suppressed hunger
  - Tonix's patented potentiated OT formulation is believed to increase activity of OT at OT receptors (OXTR)

Patents Issued

DEVELOPMENT PROGRAM

Market Entry: Treatment of hyperphagia in adolescents and young adults with Prader-Willi Syndrome

Additional Indications: Rare Hyperphagia Conditions

Status: Preclinical, granted orphan drug designation by FDA

Next Steps: pre-IND Meeting to seek agreement on development plans

*TNX-2900 is in the pre-IND stage of development and has not been approved for any indication.

TONIX PHARMACEUTICALS

Prader-Willi Syndrome (PWS)

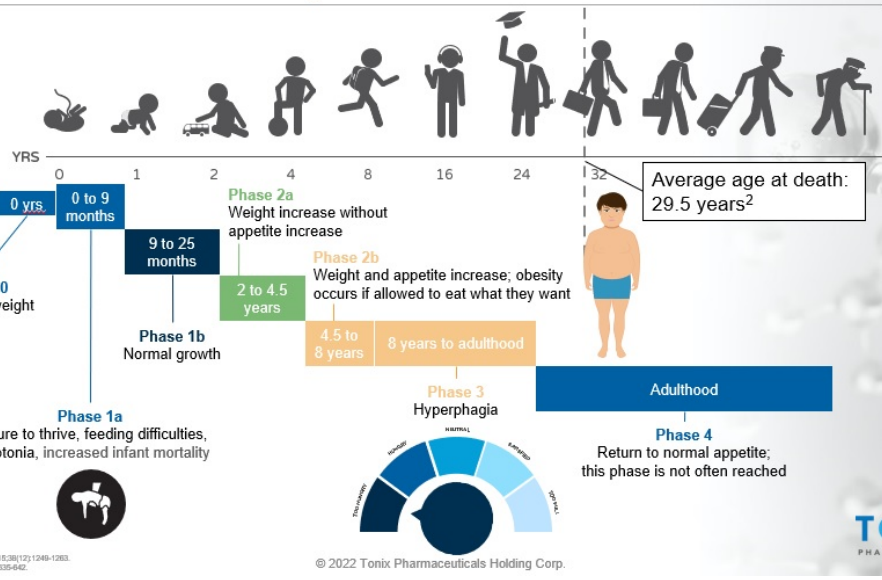
RARE DISEASE PORTFOLIO

Cause	~65% of cases are due to a new deletion on paternal chromosome 15; first genetic imprinting disorder recognized in humans
Prevalence	1 in 10,000 to 1 in 30,000[1,2]; most common syndromic cause of obesity
Symptoms	In infants, severe hypotonia and difficulty sucking. In children and adolescents, delayed global development, decreased growth resulting in short stature, intellectual difficulties, hypogonadism, hyperphagia, life-threatening obesity, behavioral problems
Diagnosis	Genetic testing: DNA methylation
Treatment	No cure, but human growth hormone treatment is FDA approved for growth failure in PWS children

[1]Angulo MA, et al. *J Endocrinol Invest*. 2019;39(12):1249-1263.
[2]McCandless, Shawn E et al. SUN-684 U.S. Prevalence & Mortality of Prader-Willi Syndrome: A Population-Based Study of Medical Claims. *Journal of the Endocrine Society*, Volume 4, Issue Supplement_1, April-May 2020, SUN–604, https://doi.org/10.1210/jendso/bvaa046.693

TONIX PHARMACEUTICALS

Progression of Prader-Willi Syndrome[1]



[1] Angulo MA, et al. *J Endocrinol Invest*. 2015;38(12):1249-1263.
[2] Butler MG, et al. *Genet Med*. 2017;19(6):635-642.

RARE DISEASE PORTFOLIO

TONIX PHARMACEUTICALS

Dangers of PWS Hyperphagia

Behaviors around food[1-4]:
- Foraging or hoarding
- Temper tantrums and meltdowns
- Binge eating
- Stealing or stealing money to buy food
- Eating garbage/spoiled food
- Obsessions and compulsions

Consequences[1-5]:
- Life-threatening obesity
- Risk of choking or gastrointestinal perforation
- Food-borne illness
- Chronic constipation
- Swallowing difficulties
- Decreased ability to vomit
- Type 2 diabetes
- Cardiovascular disease

Caretaker Burden[1-4]:
- 24/7 supervision
- Restricted food intake
- Low-calorie diet
- Locking cabinets and refrigerators

There is no treatment for PWS-related hyperphagia[4]

[1] Miller JL, et al. *Am J Med Genet A*. 2011;155A(5):1040-1049.
[2] Butler MG, et al. *Genet Med*. 2017;19(6):635-642.
[3] Butler MG. NORD. Updated 2018. Accessed May 25, 2022. https://rarediseases.org/rare-diseases/prader-willi-syndrome/
[4] Prader-Willi Syndrome Association USA. Accessed May 25, 2022. https://www.pwsausa.org/what-is-prader-willi-syndrome/
[5] Mosconi G, et al. *J Endocrinol Invest*. 2021;44(10):2067-2073.

RARE DISEASE PORTFOLIO

TONIX PHARMACEUTICALS

Abnormalities of the Oxytocin System in Patients with PWS

PWS patients have

Increased oxytocin in blood plasma[1,2]

Decreased oxytocin mRNA[1]

Low levels of oxytocin receptor expression[2]

Decreased or abnormal oxytocin neurons (especially in the PVN)[1]

PVN=paraventricular nucleus.

[1] Correia-da-Silva F, et al. *J Neuroendocrinol*. 2021;33(7):e12994.
[2] Jurek B, et al. *Physiol Rev*. 2019;99(3):1805-1868.

RARE DISEASE PORTFOLIO

TONIX PHARMACEUTICALS

History of Oxytocin Use

Synthetic oxytocin has been used to induce labor for over 65 years[1]

Due to the role of endogenous oxytocin in pain regulation and social behavior, the administration of exogenous oxytocin has been studied in a wide variety of therapeutic areas[2]

Intravenous application of oxytocin has been met with many challenges:

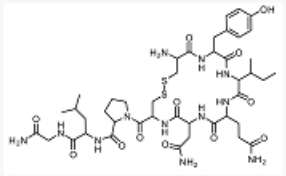
- Short half-life:
  - Intravenous oxytocin has a half-life of roughly 3 minutes[3]
- Difficulty crossing the blood-brain barrier[4]

[1] den Hertog CE, et al. *Eur J Obstet Gynecol Reprod Biol*. 2001;94(1):8-12.
[2] Bakermans-Kranenburg MJ, et al. *Transl Psychiatry*. 2013;3(5):e258.
[3] Oxytocin. Package Insert. Hikma Pharmaceuticals USA Inc.; 2011.
[4] Quintana DS, et al. *Mol Psychiatry*. 2021;26(1):80-91.

RARE DISEASE PORTFOLIO

TONIX PHARMACEUTICALS

Functions of Natural and Therapeutic Oxytocin



Childbirth[1-3]:

Natural

- Stimulates uterine contractions during childbirth

Therapeutic

- Widely used for the induction of labor in an estimated 25% of women in Western countries

Breastfeeding[1,4,5]:

Natural

- Oxytocin is responsible for the let-down reflex
- Contracts the muscles around the glands that produce milk

Therapeutic

- Approved to stimulate milk production, but discontinued in the US

Behavioral regulation[1,6]:

Natural

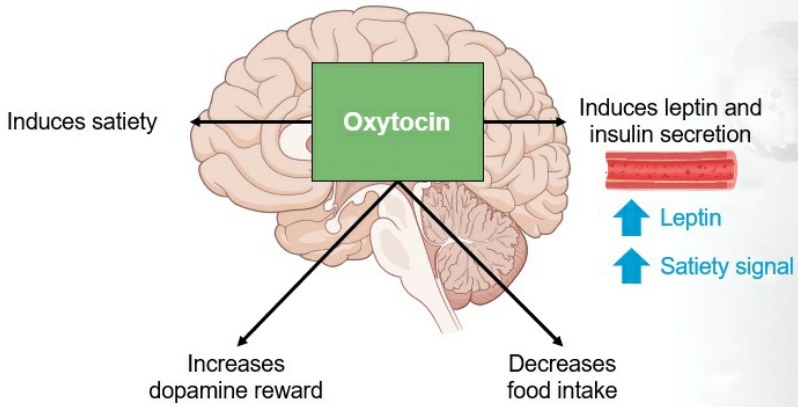
- Oxytocin plays a role in prosocial behaviors and bonding
- Signals satiety and suppresses appetite

Therapeutic

- No approved oxytocin therapy

[1] McCormack SE, et al. Endocr Rev. 2020;41(2):121-145.
[2] Kuwabara Y, et al. Arch Gynecol Obstet. 1987;241(1):13-23.
[3] Boie G, et al. Cochrane Database Syst Rev. 2018;8(8):CD012274.
[4] World Health Organization. World Health Organization; 2009. https://www.ncbi.nlm.nih.gov/books/NBK140870/
[5] MPR. December 12, 2013. Accessed June 23, 2022. https://www.empr.com/home/news/nebraphin-to-reintroduce-syntocinon-nasal-spray/
[6] Bartz JA, et al. Trends Cogn Sci. 2011;15(7):301-309.

Oxytocin Plays Major Role in Satiety[1-3]



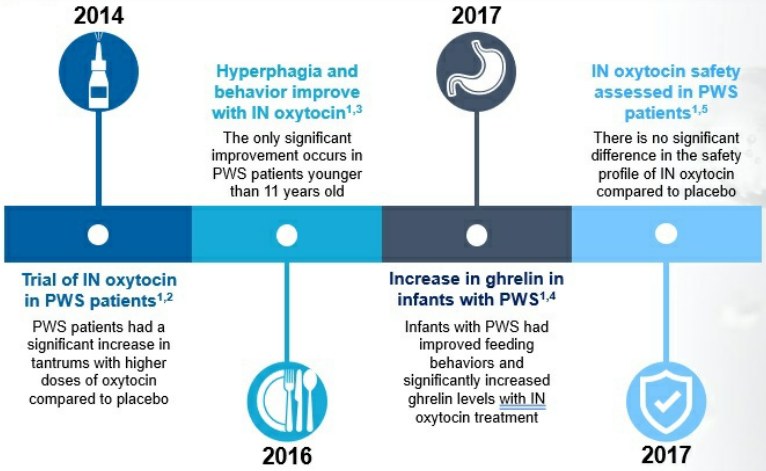
[1] Correa-da-Silva F, et al. J Neuroendocrinol. 2021;33(7):e12984.
[2] McCormack SE, et al. Endocr Rev. 2020;41(2):121-145.
[3] Karsens L, et al. Int J Mol Sci. 2021;22(14):7737.

Intranasal Use of Oxytocin

- Intranasal oxytocin was introduced as a lactation aid in the early 1960s[1]
- Numerous studies have investigated chronic and acute intranasal oxytocin for the treatment of neuropsychiatric disorders and pain[2]
  - Intranasal oxytocin has been studied in anxiety disorders,[3] autism,[4] PTSD,[5] schizophrenia,[6] and pain[7]
- Chronically administered intranasal oxytocin is generally very well tolerated[8-11]
- Intranasal oxytocin has been found to be generally safe and well tolerated in a variety of healthy populations ranging from infancy to old age[12,13]

[1] Skarsten KW. *Tidsskr Nor Laegeforen*. 1962;82:8-10.
[2] Quintana DS, et al. *Mol Psychiatry*. 2021;26(1):80-91.
[3] Jones C, et al. *Dialogues Clin Neurosci*. 2017;19(2):193-201.
[4] Quintella AJ, et al. *Eur Psychiatry*. 2010;07(7):502-504.
[5] Pitman RK, et al. *Psychiatry Res*. 1993;48(2):107-117.
[6] Feifel D, et al. *Biol Psychiatry*. 2016;79(3):222-233.
[7] Bell S, et al. *Neuroscience*. 2016;387:143-161.
[8] Rupp, Jill, et al. *Psychopharmacology (Berl)*. 2021;1-14.
[9] Horta M, et al. *Neurosci Biobehav Rev*. 2020;108:1-23.
[10] Pieger E, et al. *Neurology*. 2015;84(2):174-181.
[11] Barraza JA, et al. *Exp Clin Psychopharmacol*. 2013;21(2):85-92.
[12] DeMayo MM, et al. *Drugs*. 2017;19(5):391-410.
[13] Verhees MWFT, et al. *Psychopharmacology (Berl)*. 2018;235(8):2471-2477.

Intranasal (IN) Oxytocin As PWS Treatment



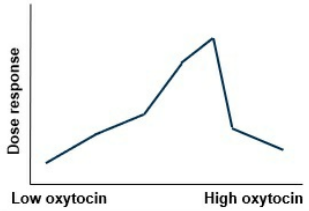
Despite strong evidence for the role of OT in satiety, there are challenges in using OT for the treatment of PWS

[1] McCormack SE, et al. *Endocr Rev*. 2020;41(2):121-145.
[2] Einfeld SL, et al. *Am J Med Genet A*. 2014;164A(9):2232-2239.
[3] Höybye C, et al. *Clin Endocrinol (Oxf)*. 2016;85(6):979-987.
[4] Tauber M, et al. *Pediatrics*. 2017;139(2):e20162976.
[5] Miller JL, et al. *Am J Med Genet A*. 2017;173(5):1243-1250.

Challenges in Intranasal Oxytocin Studies in PWS

- No significant difference with IN oxytocin treatment but significantly increased tantrums at higher doses[4]
- Significant improvement in hyperphagia but only in patients younger than 11 years old[5]

- Central oxytocin levels are difficult to measure[1]
- Dose response is not linear but an inverted-U shape[1,2]



- Recent reports show that magnesium is needed for full oxytocin receptor binding[2,3]
- Magnesium enables a full dose response[2,3]

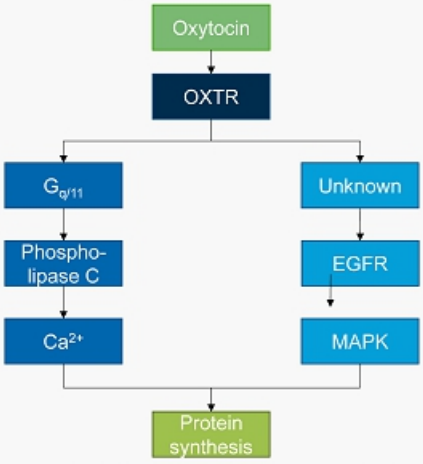
[1] Quintana DS, et al. *Mol Psychiatry*. 2021;26(1):80-91.
[2] Bharadwaj VN, et al. *Pharmaceutics*. 2022;14(5):1105.
[3] Meyerowitz JG, et al. *Nat Struct Mol Biol*. 2022;29(3):274-281.
[4] Einfeld SL, et al. *Am J Med Genet A*. 2014;164A(9):2233-2239.
[5] Miller JL, et al. *Clin Endocrinol (Oxf)*. 2016;85(6):979-987.

RARE DISEASE PORTFOLIO

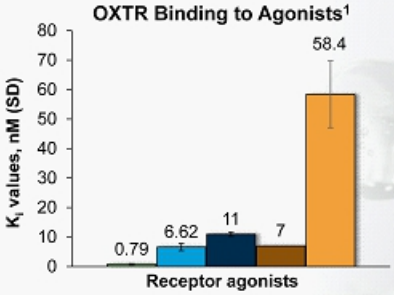
TONIX PHARMACEUTICALS

Oxytocin Receptor (OXTR)

OXTR Signaling Cascade



OXTR Binding to Agonists[1]



- Oxytocin
- TGOT = highly selective agonist
- Atosiban = functionally selective agonist (can act as an antagonist depending on the G-protein coupled to OXTR)
- Carbetocin = oxytocin analog – weak agonist with mixed antagonist activity[2]
- WAY 267,464 = nonpeptide agonist more specific for the vasopressin receptor

EGFR=epidermal growth factor receptor; MAPK=mitogen activated protein kinase; OXTR=oxytocin receptor

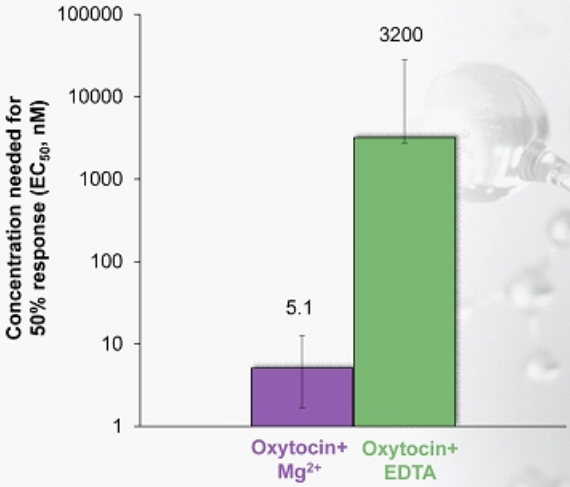
[1] Jurek B, et al. *Physiol Rev*. 2015;95(3):1805-1969.
[2] Meyerowitz JG, et al. *Nat Struct Mol Biol*. 2022;29(3):274-281.

RARE DISEASE PORTFOLIO

TONIX PHARMACEUTICALS

Oxytocin+Mg^{2+} Activates OXTR Secondary Messengers

Magnesium is needed not only for oxytocin binding to OXTR but also for OXTR activation

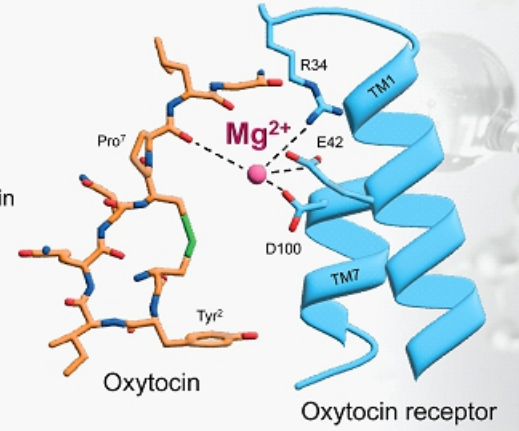


BRET assay in HEK-293 cells

BRET=bioluminescence resonance energy transfer; EDTA=etheylenediaminetetraacetic acid; HEK=human embryonic kidney; OXTR=oxytocin receptor.

Oxytocin Requires Magnesium for Receptor Binding

- OXTR exists in 2 conformational states[1]:
  - Low affinity
  - High affinity
- Magnesium ions are necessary for the high-affinity state[1,2]
- Without magnesium ions present, oxytocin cannot achieve full binding to OXTR[2]

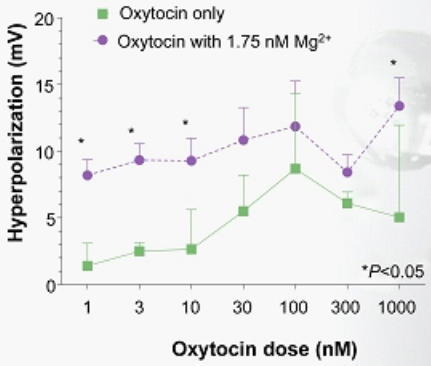


OXTR=oxytocin receptor.

[1] Janik, D. et al. *Physiol Rev.* 2010;90(3):1065-1908.
[2] Meyerowitz, JG. et al. *Nat Struct Mol Biol.* 2022;29(3):274-281.

Addition of Mg^{2+} Expands the *in vivo* Useful Dose Range of Intranasal Oxytocin in Animals

- A nonlinear dose response has been demonstrated in the use of intranasal oxytocin
- This decreases efficacy at higher doses
- Addition of Mg^{2+} rescues the efficacy of oxytocin at high doses



In vitro whole-cell voltage-clamp recordings of rat trigeminal nerves exposed to oxytocin solution with and without additional magnesium ions

Bharadwaj VN, et al. *Pharmaceutics*. 2022;14(5):1105.

RARE DISEASE PORTFOLIO

TONIX PHARMACEUTICALS

Highlights

- Hyperphagia in Prader-Willi syndrome (PWS) is severe and life-threatening
  - There is currently no treatment for hyperphagia in adolescents and young adults with PWS
- Oxytocin is one of the hormones responsible for signaling satiety
- The oxytocin receptor requires magnesium ions for the high-affinity conformation for signaling satiety
- TNX-2900* combines oxytocin with magnesium for improved receptor binding and potentially improved therapeutic action
- TNX-2900 is in development to treat hyperphagia in PWS

*TNX-2900 is an investigational drug in the pre-IND stage of development and has not been approved for any indication

RARE DISEASE PORTFOLIO

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THANK YOU
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