Halneuron®

A new approach to pain management

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WEX Pharmaceuticals | 2021

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Halneuron® is an investigational treatment and has not been approved by the US Food and Drug Administration or Health Canada or any other regulatory agencies. Halneuron® has not yet been shown to be safe and effective.

WEX Pharmaceuticals Inc. overview

Clinical-stage pharmaceutical company developing Halneuron®, a **non-opioid pain medication**, to manage moderate to severe pain

- WEX Pharmaceuticals ("WEX"), headquartered in Canada, is a pharmaceutical company focused on the development of Halneuron® for management of moderate to severe pain
- WEX is a wholly owned subsidiary of CK Life Sciences Int'l., (Holdings) Inc., a publicly listed company in Hong Kong (SEHK:0775)
- Key assets include patents on Halneuron® for Chemotherapy-Induced Neuropathic Pain and General Pain and production methods of Halneuron®

Halneuron® - A novel non-opioid pain therapy

- WEX Pharmaceuticals Inc. ("WEX") is developing a non-opioid analgesic, Halneuron®
- Tested in over 500 people. Latest clinical trials have demonstrated promising clinical results and robust safety

Halneuron®: a **non-opioid painkiller** for **moderate to severe** pain

No evidence of addiction or withdrawal symptoms, unlike opioids

Lead clinical uses in **Chemotherapy-Induced Neuropathic Pain** and **Cancer-Related Pain**

Demonstrated **clinically meaningful (>30%) pain reduction** in majority of treated patients in Phase 3 trial

Some patients experienced pain reduction for more than **30 days with 1 cycle** of treatment

Some patients experienced **30% reduction in opioid use** with 1 cycle of treatment

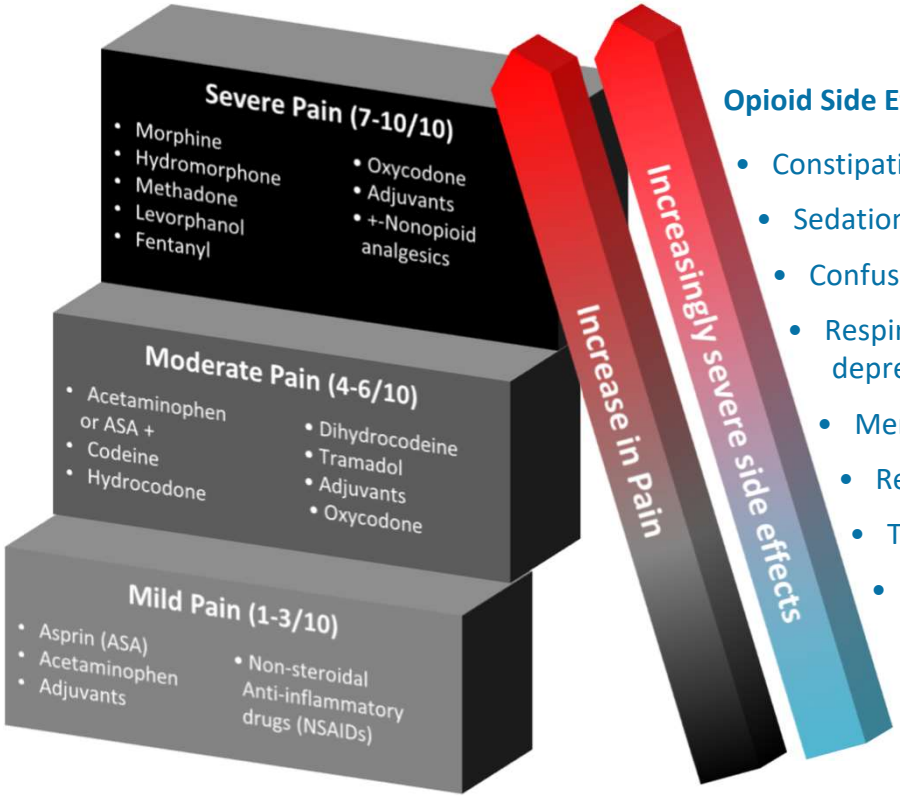
Clear pathway to **registration** and **commercialization** with **patents** and proprietary **trade secrets**

Opportunity to be the first to address a **multi-billion dollar market**

Pain therapy today: methods and challenges

- Pain treatment today is directed by side effects and tolerability
- Opioids continue to be the gold standard[1], but come with many issues and challenges

The World Health Organization Analgesic Ladder[2] and associated side effects



Opioid Side Effects[3]

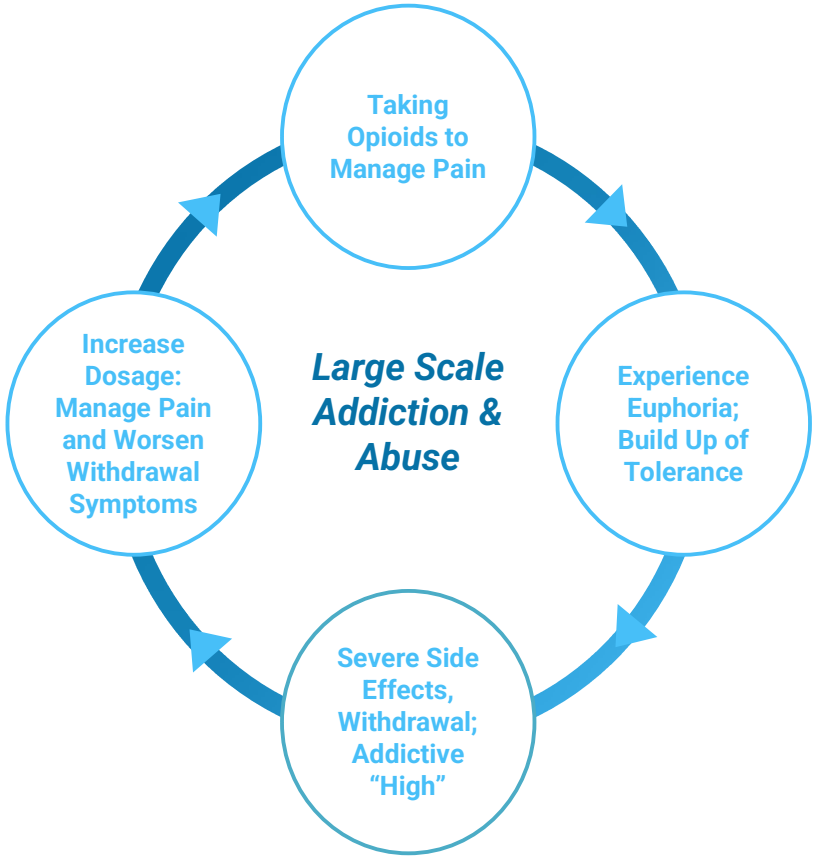
- Constipation
- Sedation
- Confusion
- Respiratory depression
- Mental clouding
- Renal colic
- Tolerance
- Abuse, misuse
- Addiction

There is a large and unmet need for new non-opioid neuropathic and nociceptive agents due to side effects and abuse of current therapies.

Notes:

1. Li JX. Combining opioids and non-opioids for pain management: Current status. Neuropharmacology. 2019 Nov 1;158:107619.
2. Harris DG. Management of pain in advanced disease. Br Med Bull. 2014 Jun;110(1):117-28.
3. Benyamin R, Trescot AM, Datta S, Buenaventura R, Adlaka R, Sehgal N, Glaser SE, Vallejo R. Opioid complications and side effects. Pain Physician. 2008 Mar;11(2 Suppl):S105-20.

Vicious cycle with opioid pain therapies



Opioid-based painkillers are today's gold standard to manage moderate to severe pain

While effective at managing pain, opioids have numerous concerning issues:

- **Highly addictive,** a recognized public health crisis
- **Severe side effects**
- **Withdrawal symptoms** prevent reducing dosage
- Addiction, withdrawal symptoms, and side effects worsens as potency increases to manage long-term and chronic pain conditions

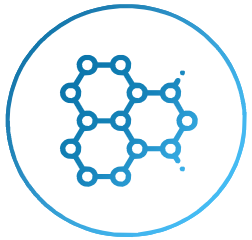
- Over 53,000 opioid deaths in the past 12 months in the US alone[1]
- ~58 million people used opioids and ~35.6 million people suffered from drug use disorders worldwide in 2018[2].

There is an urgent need for a non-addictive analgesic to substitute opioid-based pain therapies.

Notes:

1. CDC - https://www.cdc.gov/nchs/nvss/vsrr/drug-overdose-data.htm
2. WHO - https://www.who.int/news-room/fact-sheets/detail/opioid-overdose

Halneuron® - Fulfils the requirements of an ideal analgesic



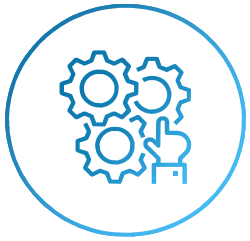
No evidence of addiction

No evidence of euphoria, or "high"

No evidence of tolerance build with repeated use

Evidence of long-lasting pain relief

No evidence of withdrawal symptoms



Cost effective, can be produced at scale

Acceptable safety profile with only mild and temporary side effects

Based on promising research and results to-date, Halneuron® is well-positioned to be a credible alternative to manage pain.

Notes:

1. WEX-002, WEX-14OL, TEC-006OL, TEC-006, WEX-CINP-201, WEX-CINP-201PK and other WEX conducted clinical trials

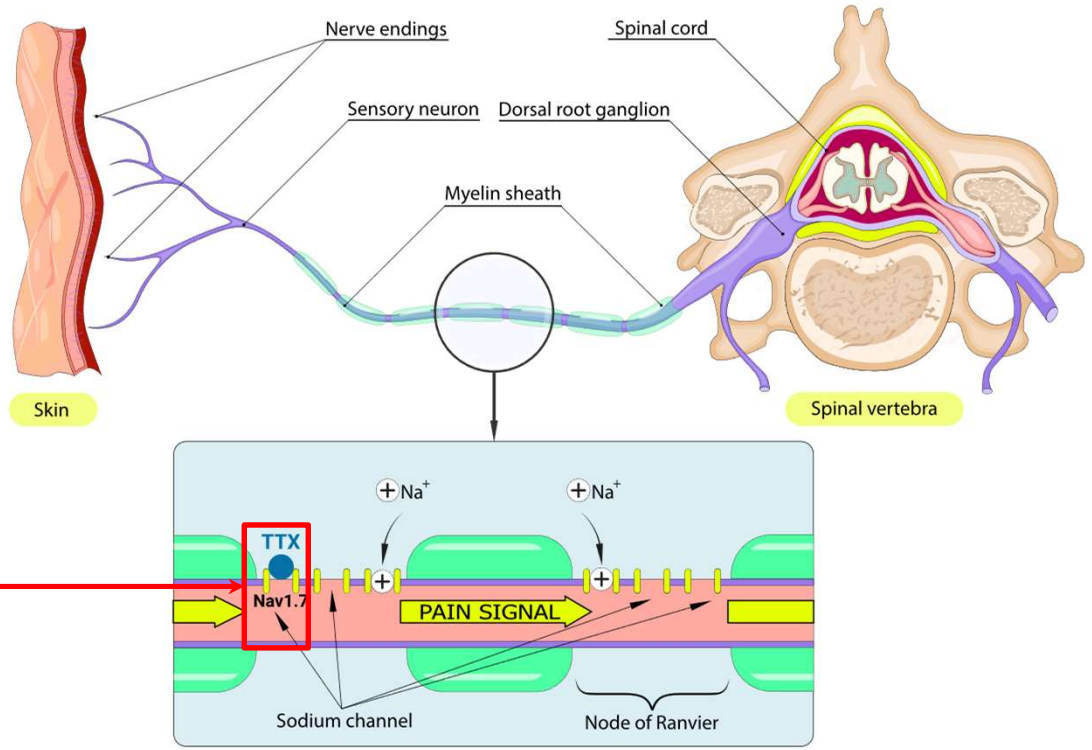
What is Halneuron®?

- Halneuron® is Tetrodotoxin (TTX), a sodium channel blocker
- TTX works as a painkiller by blocking NA_V 1.7, a sodium channel responsible for pain
- TTX binding and blocking NA_V 1.7 are well understood[1,2]

How does Tetrodotoxin (TTX) work?

Pain signals are nerve impulses that travel along a nerve as electrical signals generated by the movement of sodium ions through ion channels on the surface of nerve cells.

TTX binds to and blocks sodium ion channels on the nerve cell surface, reducing the movement of sodium ions, thereby reducing the conduction of pain signals.



Notes:

1. Fozzard HA, Lipkind GM. The tetrodotoxin binding site is within the outer vestibule of the sodium channel. Mar Drugs. 2010 Feb 1;8(2):219-34.
2. Nieto FR, Cobos EJ, Tejada MÁ, Sánchez-Fernández C, González-Cano R, Cendán CM. Tetrodotoxin (TTX) as a therapeutic agent for pain. Mar Drugs. 2012 Feb;10(2):281-305.

Na_V 1.7 is directly associated with the feeling of pain

- The sodium channel Na_V 1.7 is responsible for the perception of pain. This is well supported in peer-reviewed research over the past decades[1,2,3]
- Two health conditions associated with abnormal expression of Na_V 1.7 and their effects on the perception of pain is well-documented

Feel No Pain

Congenital Insensitivity to Pain Syndrome:

- Rare genetic mutation that causes an **absence** of a **Na_v 1.7 sodium channel**
- Condition that prevents the ability to perceive pain

Hypersensitivity to Pain

Erythromelalgia: Severe Pain Syndrome

- Hypersensitivity to pain
- **Mutations** in the sodium channel **Na_v 1.7** produce **pain syndromes**
- Characterized by feeling **intense, burning pain** primarily affecting one's feet and hands

Authoritative research and known health conditions related to Na_v 1.7 provide strong evidence that blocking Na_v 1.7 is a critical pathway to blocking and alleviating pain.

Notes:

1. Dib-Hajj SD, Yang Y, Black JA, Waxman SG. The Na(V)1.7 sodium channel: from molecule to man. Nat Rev Neurosci. 2013 Jan;14(1):49-62.
2. Han C, Rush AM, Dib-Hajj SD, Li S, Xu Z, Wang Y, Tyrrell L, Wang X, Yang Y, Waxman SG. Sporadic onset of erythermalgia: a gain-of-function mutation in Nav1.7. Ann Neurol. 2006 Mar;59(3):553-8.
3. Faber CG, Hoeijmakers JG, Ahn HS, Cheng X, Han C, Choi JS, Estacion M, Lauria G, Vanhoutte EK, Gerrits MM, Dib-Hajj S, Drenth JP, Waxman SG, Merkies IS. Gain of function Nav1.7 mutations in idiopathic small fiber neuropathy. Ann Neurol. 2012 Jan;71(1):26-39.

Latest clinical trials investigating Halneuron®

- Studies using Halneuron® for managing pain have shown encouraging clinical results
- Lead indications for Halneuron® include two recent clinical trials:
  - Phase III **Cancer Related Pain** (“**CRP**”)
  - Phase II **Chemotherapy-Induced Neuropathic Pain** (“**CINP**”). Currently there are no approved drugs for managing CINP.

Phase III Cancer Related Pain

- Tested for **efficacy** and **safety of TTX** for moderate to severe inadequately controlled **CRP**
- Randomized, double-blind, placebo-controlled, parallel-design, multicenter, trial
- **Patients enrolled:** 165
- **Statistically significant** difference in Responder Rates, based on pain reduction

- Some patients demonstrated **pain relief for more than 30 days** post injection period
- TTX showed an acceptable safety profile in cancer patients.

Phase II Chemotherapy-Induced Neuropathic Pain

- Primarily a dose finding trial but also evaluating potential efficacy and safety of TTX in patients with **CINP**
- Randomized, double-blind, dose-finding, placebo-controlled, multicenter study
- **Patients enrolled:** 125

- Optimal therapeutic dose to treat CINP established
- TTX showed an acceptable safety profile in CINP patients.

Phase III CRP: Clinical trial design

- All patients were on standard of care[3] for pain management, half receiving Placebo and the other half receiving TTX
- TTX treatment involved 2 injections a day for 4 days (8 doses total)
- All patients recorded their pain score in two distinct periods with extended follow up:
  - Pain response first measured from days 5 to 8 post injection (Early Post-Injection Period)
  - Pain response also measured from days 9 to 15 post injection (Late Post-Injection Period)
  - Follow up conducted after late post-injection period to measure any prolonged effects from TTX on pain

Phase III CRP - Patient Population

	TTX [1]	Placebo [2]	Total	
Number of Patients Enrolled	77	88	165	100%
Patients Treated	65	84	149	90%
Patients Enrolled with Severe Pain	68	76	144	87%
Average Pain Score Before Treatment	7.6	7.6		

Notes:
1. TTX + Standard of care for pain management.
2. Placebo + Standard of care for pain management.
3. Standard of care for pain management is defined as optimized opioid and co-analgesic therapy specific to each patient.

Phase III CRP: Pain measurement outcome

- There was a statistically significant improvement in pain outcome for TTX
  - 51% of patients receiving TTX experienced a reduction in pain; vs
  - 35% of patients in the placebo group recorded a reduction in pain

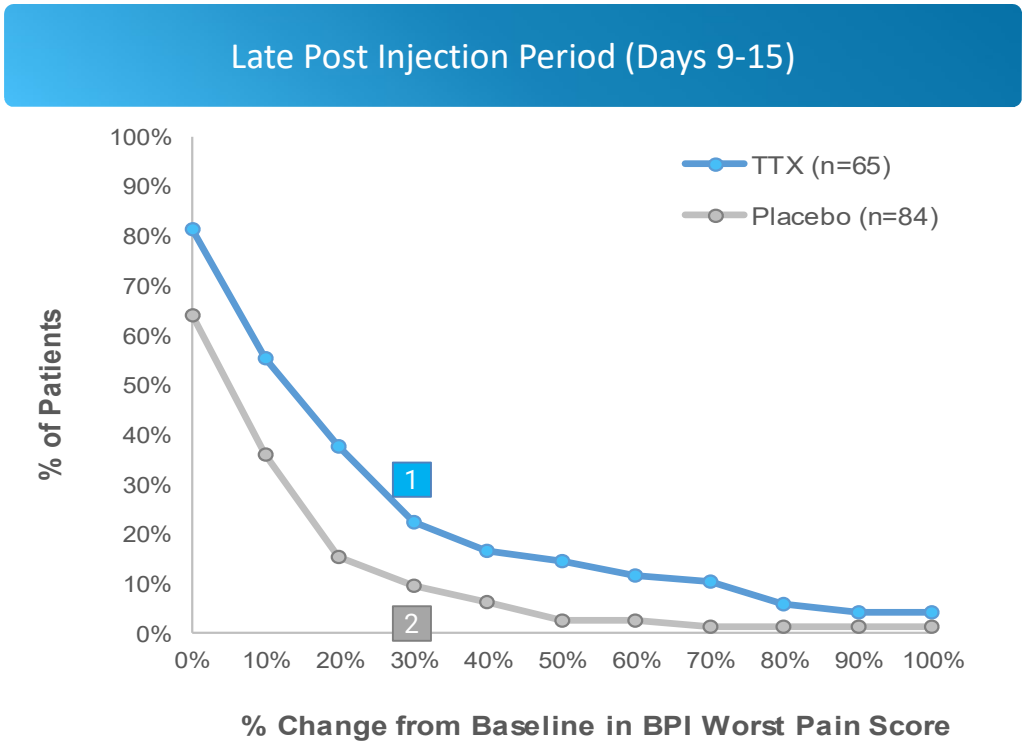
Pain Outcome – Co-Primary Endpoint
(Pain Intensity Difference and/or Opioid Use)

	TTX [1]		Placebo [2]		Difference
Responder [3]	33	*51%*	29	*35%*	16%
Non-Responder	32	*49%*	55	*65%*	
Total	**65**		**84**		
95% C. I.	0.4 - 32.1				
p-value	**0.046**				

Notes:
1. TTX + Standard of care for pain management.
2. Placebo + Standard of care for pain management.
3. A "Responder" is defined as a patient who has a mean reduction in pain intensity of ≥ 30%; or a decrease of at least 50% of opioid use.

Phase III CRP: TTX reduced worst pain

- There were more patients that demonstrated at least 30% pain reduction in the TTX treatment group over the Placebo group
- Furthermore, using any percentage of pain relief, TTX always demonstrated greater pain reduction over Placebo.



% of patients in group showing **≥30% reduction in BPI[2] Worst Pain Score** in LPIP:

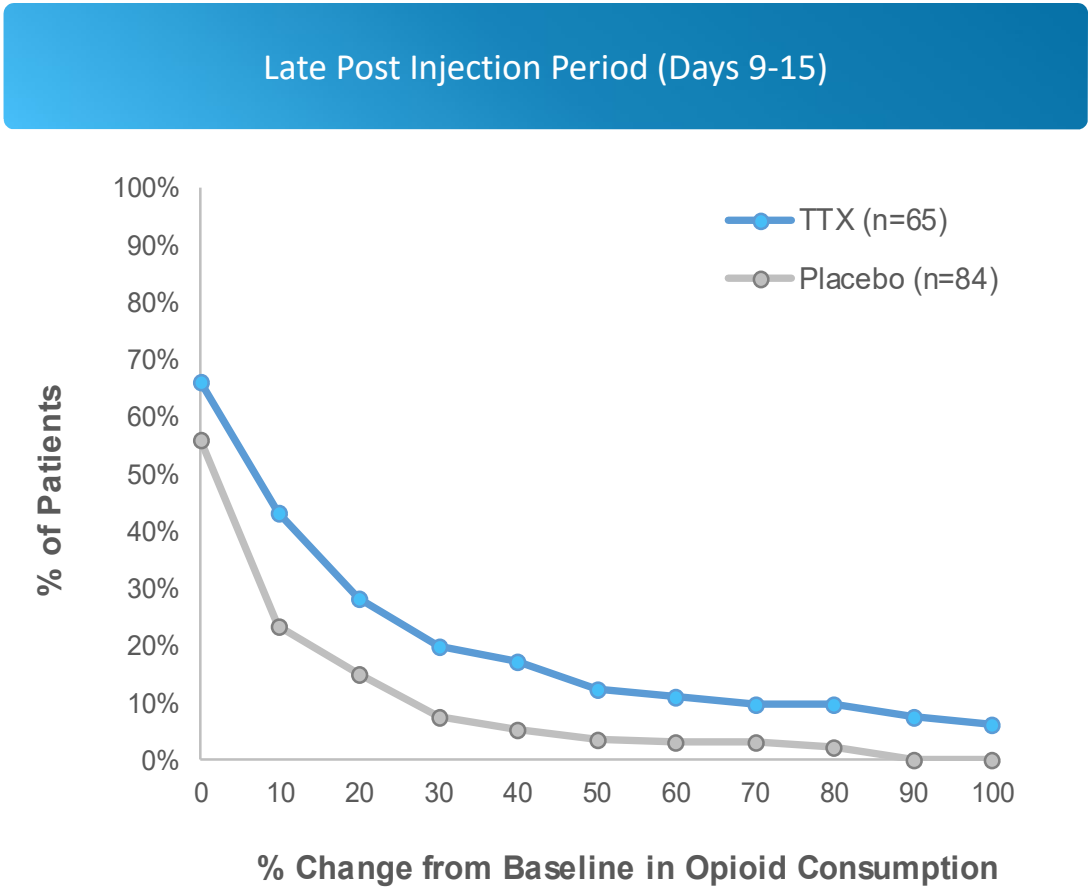
1 **21.5%** of patients on TTX, vs

2 **8.3%** of patients on Placebo

Notes: 1. TTX means TTX + Standard of care for pain management. Placebo means placebo + Standard of care for pain management.
2. BPI means Brief Pain Inventory which is a medical questionnaire used by patients to measure the severity of their pain.

Phase III CRP: TTX reduced opioid consumption

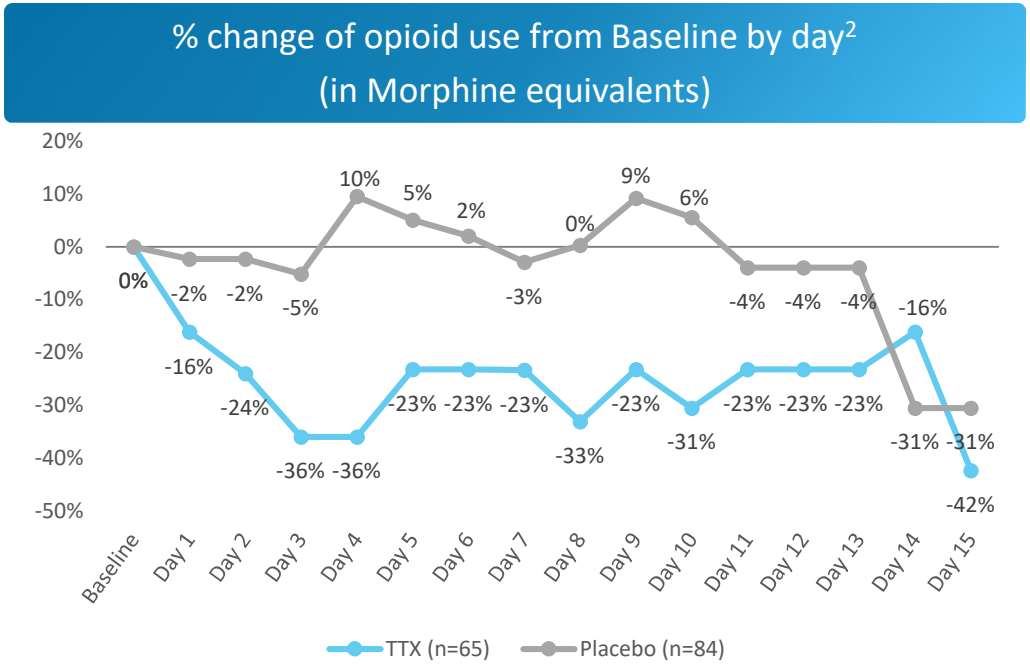
- Using any percentage in reduction of opioid consumption, there were more patients in the TTX group who reduced their opioid intake during the clinical trial than in the Placebo group.



Notes: 1. TTX means TTX + Standard of care for pain management. Placebo means placebo + Standard of care for pain management.

Phase III CRP: TTX reduced daily opioid use[1]

- Patients in the TTX group demonstrated an immediate and consistent reduction in opioid use
- Encouraging evidence that patients on TTX experienced sufficient pain reduction to reduce their daily use of opioid pain medication



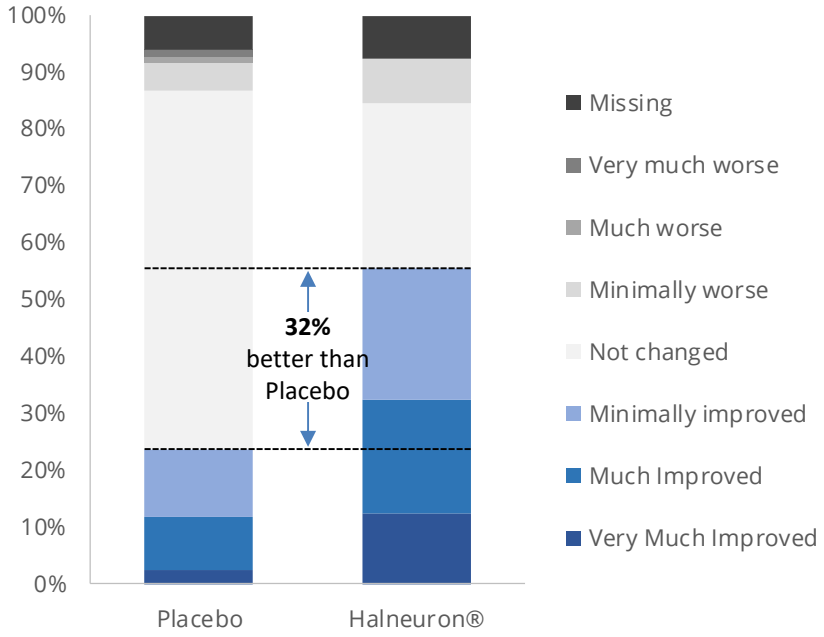
- Placebo patients had no meaningful reduction in daily opioid use for most of study period
- TTX patients demonstrated meaningful and sustained reduction in daily opioid consumption

Note:

1. Opioid use is defined as the average dose, converted to morphine equivalents, as reported on the patient diary, during each treatment period.
2. In the "Intent to Treat" population

Phase III CRP: Global Impression of Change

Patients in the TTX group reported an improvement in pain compared to the placebo group



	Halneuron® [1]	Placebo [2]	No. of times better than Placebo
Very Much Improved	12%	2%	6X
Much Improved	20%	10%	2X
Minimally improved	23%	12%	2X
Total Improved	**55%**	**24%**	**2X**
Not changed	29%	63%	
Minimally worse	8%	5%	
Much worse	0%	1%	
Very much worse	0%	1%	
Missing	8%	6%	

55% of patients on TTX reported improvement vs 24% of patients on placebo

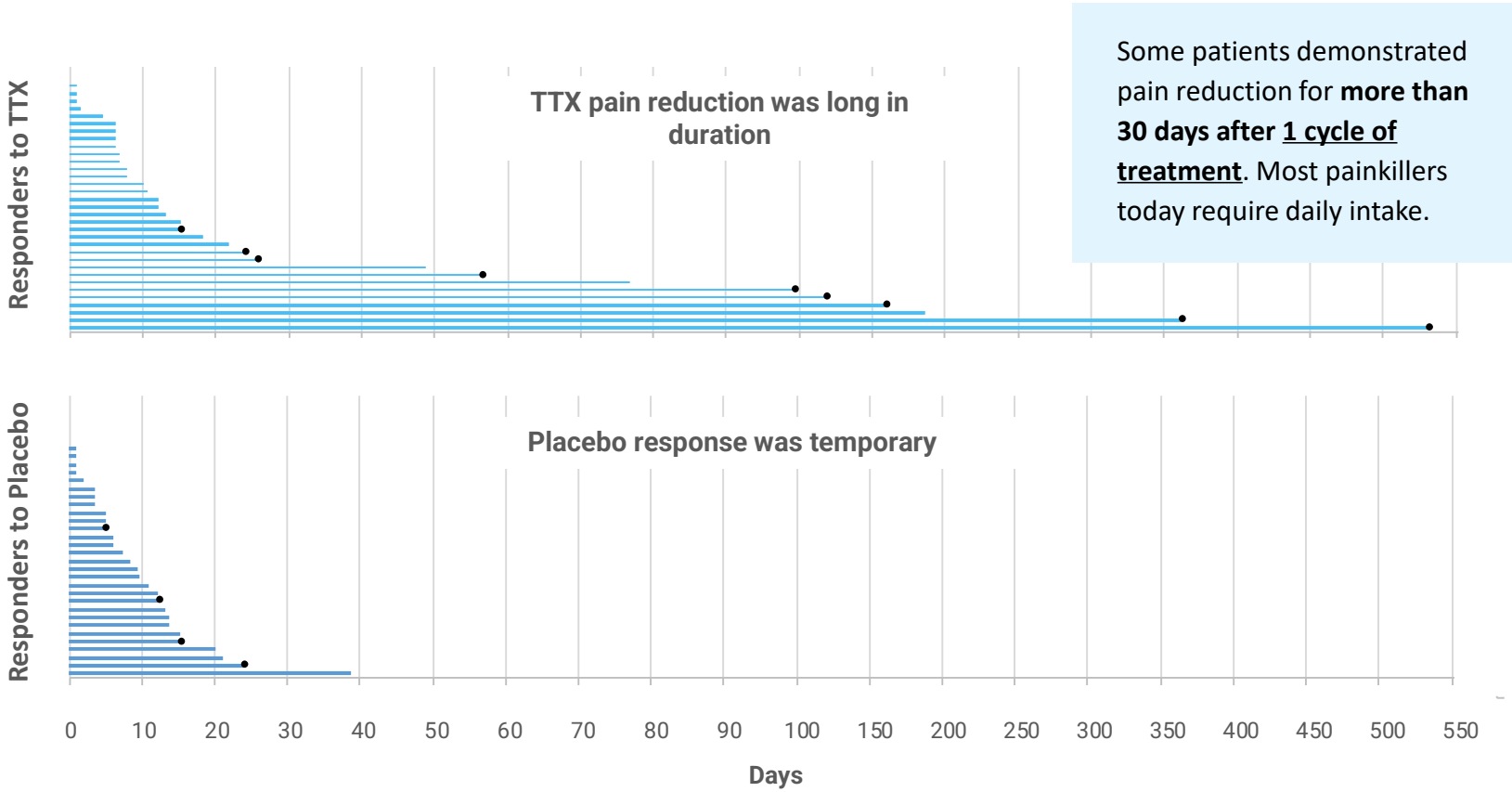
70% of patients on placebo reported no change or worse pain vs 37% of patients on TTX

Notes:

1. TTX + Standard of care for pain management.
2. Placebo + Standard of care for pain management.
3. Standard of care for pain management is defined as optimized opioid and co-analgesic therapy specific to each patient.

Phase III CRP: Long duration of pain relief

- After a single cycle of treatment, the Responders[1] in the TTX group showed a **prolonged duration** of pain relief that was **substantially longer** than the Responders[1] in the Placebo group
- Average number of days of pain response is 57.7 days vs 10.5 days for the TTX vs Placebo groups respectively
- 9 patients (27%) in the TTX Responder[1] group had pain relief for 30 days or longer after the initial injection period



Some patients demonstrated pain reduction for **more than 30 days after 1 cycle of treatment**. Most painkillers today require daily intake.

Notes:

1. A "Responder" is defined as a patient who had a mean reduction in pain intensity of ≥ 30% or a decrease of at least 50% of opioid use.
2. Dots at the end of lines indicated responses still ongoing at the end of the study, so actual duration was likely longer.

Phase II CINP: Trial summary

- WEX completed a Phase II CINP study with TTX
  - Randomized, double-blind, dose-finding, placebo-controlled, multicenter study of the potential efficacy and safety of TTX in patients with Chemotherapy-Induced Neuropathic Pain (CINP)
- Objective
  - Primary objective was to identify up to 2 doses or regimens of TTX for Phase III evaluation
  - Secondary objective was to determine the safety and tolerability of multiple doses / regimens of TTX
- Procedures
  - Testing period of various doses over 4 days and measurement over 4 weeks
  - Total of 125 patients in 5 cohorts (4 groups with different TTX dosing regimens and 1 placebo group)
- Results
  - Dosage of 30 µg TTX twice per day (for 4 days) demonstrated highest level of pain reduction vs placebo
  - This trial demonstrated an acceptable safety profile in patients with CINP.

Responder Analyses: 30% reduction in average NPRS[1] score from baseline to any 10 consecutive days

	TTX [2]	Placebo [3]
Yes	15 (58%)	8 (32%)
No	11 (42%)	17 (68%)
P-Value	**0.027**	
Odds Ratio (vs Placebo)	3.9	
95% CI for Odds Ratio	(1.08, 14.09)	

Notes: 1. Numeric Pain Rating Scale. 2. TTX + Standard of care for pain management. 3. Placebo + Standard of care for pain management. Standard of care for pain management is defined as optimized opioid and co-analgesic therapy specific to each patient.

Phase 2 CINP Clinical trial supports Halneuron® safety

- **99.0% of the Adverse Events (AEs) were mild or moderate in severity**
- **AEs were short in duration with no intervention needed**
- **No opioid like AEs**
- **There were no reported serious drug related AEs**
- **Two subjects discontinued because of AEs (vertigo)**

Ten most frequent Adverse Events [1]

Adverse event	(30 µg b.i.d. x 4 d) # Subjects (%) N=26	Placebo # Subjects (%) N=25	Delta
Paraesthesia oral	11 (42.3)	3 (12.0)	8 (30.3)
Hypoaesthesia oral	10 (38.5)	3 (12.0)	7 (26.5)
Headache	9 (32.6)	5 (20.0)	4 (12.6)
Dizziness	8 (30.8)	5 (20.0)	3 (10.8)
Paraesthesia	7 (26.9)	6 (24.0)	1 (2.9)
Nausea	6 (23.1)	6 (24.0)	0 (-0.9)
Pain in extremity	3 (11.5)	2 (8.0)	1 (3.5)
Dysgeusia	3 (11.5)	0 (0.0)	3 (11.5)
Fatigue	3 (11.5)	4 (16.0)	-1 (-4.5)
Oral dysesthesia	2 (7.7)	0 (0.0)	2 (7.7)
Injection site pain	1 (3.8)	0 (0.0)	1 (3.8)

Other clinical trials with patients and healthy volunteers have also demonstrated that Halneuron® has an acceptable safety profile and is well tolerated after multiple doses.

Notes: 1. Adverse Events ranked by Preferred Term

Halneuron® has a pipeline of other potential clinical uses

- In addition to treating Chemotherapy-Induced Neuropathic Pain and Cancer Related Pain, Halneuron® can potentially be used to manage other types of pain

Pre-Clinical	Phase I	Phase II	Phase III	Commercialization

HALNEURON® Injectable:
Chemotherapy-Induced Neuropathic Pain

HALNEURON® Injectable:
Cancer Related Pain

HALNEURON®
Burn Pain

HALNEURON®
Post-operative pain

In the near term, WEX is focused on advancing Halneuron® for managing three types of pain: CINP, Cancer Related Pain, and Burn Pain.

Advancing Halneuron® to treat pain

- WEX can pursue multiple paths to advance TTX to potentially treat CINP and CRP

Phase IIB CINP (optional)

- Phase IIB trial is specifically designed to study the efficacy of Halneuron® in a smaller population
- Trial will reduce risk and hone the Phase III trial
- Phase IIB is optional; can proceed to Phase III directly

Phase III CINP Regulatory Status

- Health Canada CINP clinical protocol: Approved
- Food and Drug Administration (FDA) Special Protocol Assessment (SPA) For Phase III trial: Approved
- European Medicines Agency (EMA) scientific review: Completed
- Cardiac safety (TQT study): Completed successfully

Phase III CRP Regulatory Status

- Cancer Related Pain SPA is in progress

Management team and leadership

- WEX's leadership team has a strong track record and experience in the life sciences and other industries:

Walter Korz, MBA
COO

- Over 35 years of multi-disciplinary experience in healthcare and life science companies
- Broad drug development background: clinical development, business development, finance, regulatory affairs
- VP Drug Development, and President and CEO of Chemokine Therapeutics
- Clinical Development Manager, Angiotech Pharmaceuticals, overseeing systemic therapy programs for rheumatoid arthritis, psoriasis, multiple sclerosis
- Cancer research at AltaRex Corp, Biomira Research

Andrew Buckland
CFO

- Over 15 years of experience as most senior financial officer of US public and pre-IPO life sciences companies
- Diverse background in international business and experienced financial officer
- CFO, PURE Bioscience, Inc., grew from the OTC Bulletin Board to the NASDAQ Stock Exchange
- VP of Finance, Cardionet, Inc.
- CFO, Advanced Tissue Sciences, Inc., NASDAQ-listed public biotechnology company
- Senior accounting and finance management positions at Bristol-Myers Squibb and United Parcel Service.

Dr. Meng Zhou
VP Manufacturing

- Over 19 years of pharmaceutical industry experience, focusing on drug delivery, formulation development, analytical chemistry, natural product research, supply manufacturing, and commercialization
- Sr. Director of R&D, SteriMax Inc., specialized in injectable product development
- Directed PDS group in Contract Pharmaceutical Limited, NDA, ANDA and 505(b)2 projects from a global client base.
- Research scientist, Patheon Inc., Endo Pharmaceuticals, and ALZA Corporation (J&J Company)
- PhD in Pharmaceutical Science, University of Georgia (2001); MS in Technology Management, Steven Institute of Technology (2007), BS in Medicinal Chemistry from Beijing Medical University (1997)

Abner Yong, CPA, CA
VP Finance

- Over 15 years of corporate finance, accounting, reporting, tax, treasury and transactions experience
- Senior accounting and finance positions held with responsibilities in global treasury, accounting, budgeting at Methanex Corporation, NASDAQ/TSX listed (BBB-/Baa3) multinational chemicals company
- Corporate transactions, Debt financing, corporate restructuring transactions, Ernst & Young Transactions Advisory Services

Halneuron® - A novel non-opioid pain therapy

- **Halneuron®:** non-opioid pain therapeutic
  - Highly differentiated by mechanism of action and avoidance of opioid associated side effects

- **Lead indications:** Chemotherapy-Induced Neuropathic Pain (CINP) and Cancer-Related Pain (CRP)
  - Currently there is no treatment specifically approved for Chemotherapy-Induced Neuropathic Pain
  - CINP and CRP markets are expected to be ~$1.5 billion[1,2] in the 7 major markets and ~$5 billion[3] globally per year respectively

- **Validated Mechanism:** Pain blocking process well-validated by decades of scientific research
  - Latest trials on patients with CRP and CINP further validate academic research

- **Clear Regulatory Path:** Phase III Special Protocol Assessment approved by FDA and Health Canada, clearing all hurdles for Phase III trial
  - Clear pathway to commercialization with established patents and manufacturing process

- **Experienced Leadership:** Track record of success, developing compounds from clinic to market

Notes:

1. Delveinsight December 2018, Chemotherapy-Induced Peripheral Neuropathy, Market insights, Epidemiology and Market Forecast 2018-2027
2. Datamonitor Healthcare, Neuropathic Pain, 16 Match 2018 and 17 May 2018,
3. Allied Market Research December 2018, Global Cancer Pain Market, Opportunity Analysis and Industry Forecast 2018-2025

Halneuron®

A new approach to pain management

walterk@wexpharma.com

WEX Pharmaceuticals | 2021

POTENTIAL TRANSACTION OPPORTUNITIES

Transaction opportunities

- WEX Pharmaceuticals is seeking a partner to advance the development of Halneuron®
- Deal structures considered: licensing, joint venture, options, royalty, contingent payments
- Open to transacting for each indication on a standalone basis or a combination
- Open to transacting for a specific or a collection of geographic markets

Indication	**Chemotherapy-Induced Neuropathic Pain**	**Chemotherapy-Induced Neuropathic Pain**	**Cancer Related Pain**
Progress To-Date	Phase IIA complete	Phase IIA complete; and Phase III trial design and Health Canada approval and FDA (Special Protocol Assessment (SPA)) approved	Phase II complete; Early Phase III
Next Milestone	Phase IIB clinical trial (Optional)	Phase III clinical trial	Phase III clinical trial
Investment Required (USD)	$7m	$30m	$30m

Halneuron® presents an attractive entry point for any company seeking a strong asset with an expeditious timeline for significant value creation.