



EVOKE
P H A R M A

NASDAQ: EVOK
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Product

- Gimoti™: a novel nasal spray delivery of metoclopramide
- Relief of symptoms in adult women with acute and recurrent diabetic gastroparesis

Large, Growing & Unsatisfied Market

- 12-16M patients in US, 80% female, poorly served with limited efficacy from current standard of care
- Only 1 FDA-approved product: metoclopramide (oral & injection)
- ~4M prescriptions annually for oral metoclopramide

Differentiation versus Oral Medications

- Bypasses the GI tract and enters the bloodstream directly
- Predictable absorption despite delayed and erratic stomach emptying
- Absorption not affected by vomiting

Compelling Commercial Opportunity

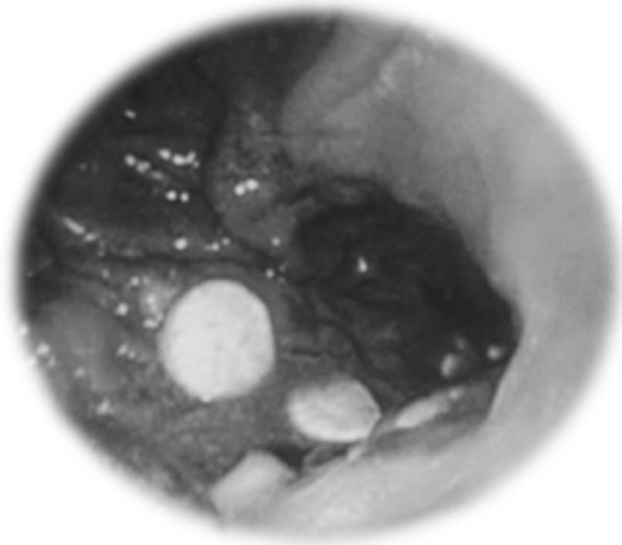
- Peak sales potential of several hundred million dollars depending upon pricing and sales force sizing
- Few expected reimbursement impediments
- Targeted GI specialty sales force of less than 100 FTE's

Clear Regulatory Pathway

- Positive comparative exposure PK trial results announced October 2017
- Sex-based PK differences for Gimoti announced in February 2018
- FDA Pre-NDA meeting held January 2018 for female-only filing strategy
- **NDA submitted June 1, 2018; acceptance for review expected in August**

Unpredictable symptom flares can lead to costly hospitalizations

Undissolved drug tablets in stomach



Simpson, S.E., Clinical Toxicology, 2011

- Delayed emptying of stomach contents to small intestine (in the absence of an obstruction) interferes with oral absorption
- Vomiting further complicates effectiveness of oral medications
- Signs and symptoms characteristic of flare:

Nausea

Abdominal Pain

Early Satiety

Bloating

Prolonged Fullness

Vomiting

Impact on patients:

Diminished Quality of Life • Malnourishment • Poor Diabetes Control • Hospitalizations (Avg. 6+ days*)

* Wang, YM. Am J of Gastroenterol 2008; 103:313-322



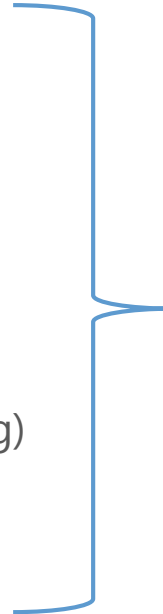
12 – 16 million patients with symptoms of gastroparesis and one FDA approved drug

- **80% of diabetic gastroparesis patients are women**
 - Diabetes is #1 known cause of gastroparesis
 - ~2-3M patients currently receive treatment
 - Under-diagnosed in part due to lack of awareness
 - Prevalence increasing due to growing diabetes population
- **Estimated \$3-4B prescription market**
- **\$3.5B in additional hospitalization costs in 2004**

- Wang, Parkman. "Gastroparesis Related Hospitalizations in the United States: Trends, Characteristics and Outcomes 1995-2004" *AM J Gastroenterol* 2008; 103:313-322
- Samsom M, Roelofs J. "Prevalence of Delayed Gastric Emptying in Diabetic Patients and Relationship to Dyspeptic Symptoms." *Diabetes Care*, Vol. 26, No. 11, Nov. 2003, 3116-3122
- Hasler WL. *Current Gastro Reports* 2007; 9: 261-269
- Intagliato NI, Koch KL. *Current Gastro Reports*
- Soykan I, Sivri B, Sarosiek I, Kiernan B, McCallum RW. Demography, clinical characteristics, psychological and abuse profiles, treatment, and long-term follow-up of patients with gastroparesis. *Dig Dis Sci* 1998;43:2398-404

Current oral treatment options lack predictable delivery and absorption, leading to inadequate treatment

- **Motility & Symptoms**
 - Oral Metoclopramide (1st line)
 - Domperidone (not FDA-approved)
- **Motility**
 - Erythromycin (used off-label)
- **Symptoms**
 - Odansetron, promethazine (nausea & vomiting)
 - PPI's (abdominal pain)
 - Narcotics (abdominal pain)



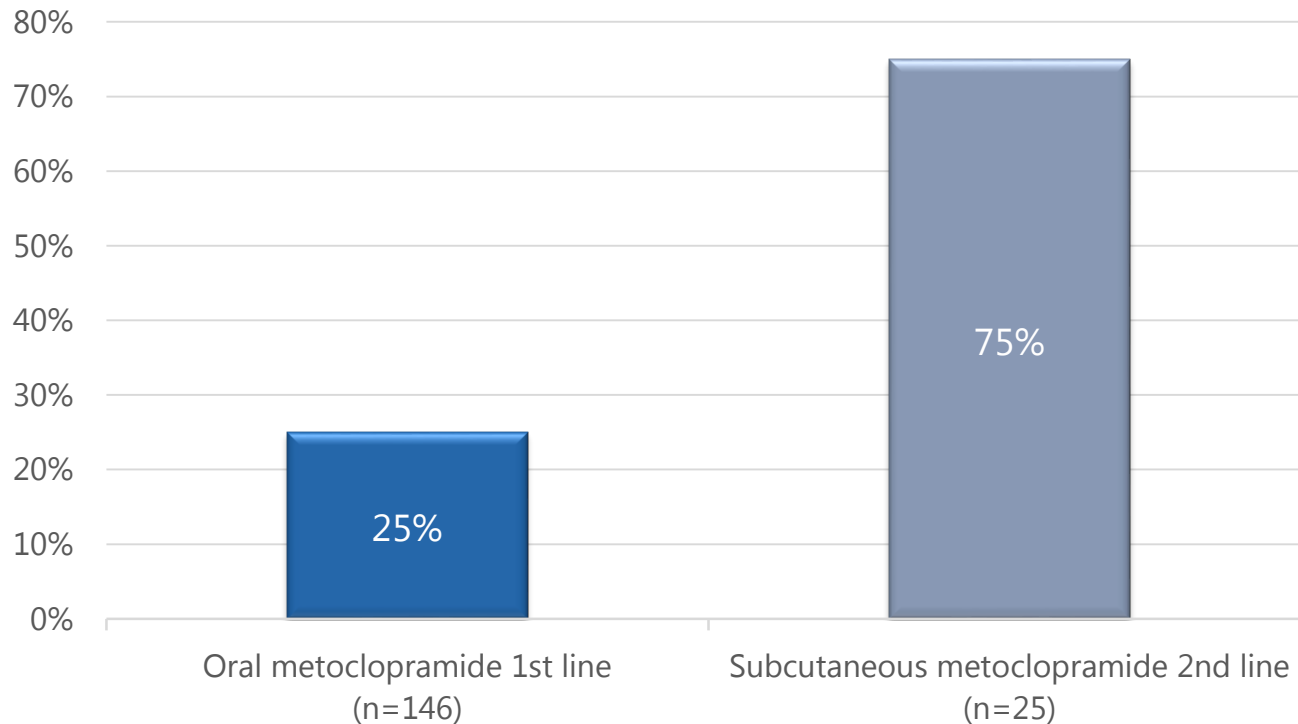
Ineffective Treatments and Inadequate Response

- Erratic absorption of oral drugs* (significant delay, multi-dose dumping) or no absorption due to vomiting
- Unpredictable efficacy and potential safety concerns
- Lack of compliance due to nausea and other GI symptoms

* Gastroparesis: Clinical Evaluation of Drugs for Treatment FDA Guidance for Industry. July 2015

Success rate for alternative administration shown to be 3x higher than oral

Metoclopramide gastroparesis success rates by delivery route at a GI motility clinic



- “This non-oral route generates a constant plasma level of the metoclopramide when:
 - Patients are vomiting
 - Unpredictable absorption limits the value of any orally administered agent”
- Clinical study only: Subcutaneous metoclopramide not commercially available and not FDA approved

Soykan. et al Digestive Diseases and Sciences, Vol. 43, No. 11 (November 1998)

Novel approach for symptomatic relief of acute & recurrent diabetic gastroparesis in women

Spray delivered and absorbed in the nasal cavity



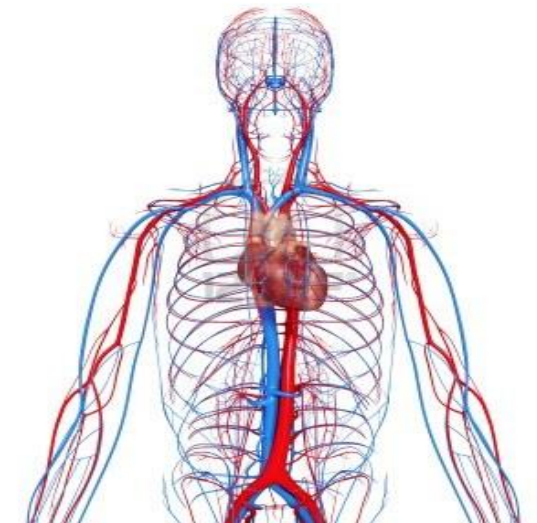
Gimoti™

(metoclopramide nasal spray)



Provides:

- Predictable absorption regardless of gastric emptying delays
- Symptom relief even during flares



Unlike oral medications, nasal delivery:

- Bypasses the GI tract to directly enter the bloodstream
- Ensures predictable absorption despite vomiting and gastric emptying delays

Compelling Commercial Opportunity

Significant Unmet Need

- Physicians and patients report broad interest in non-oral treatment alternatives to address unpredictable absorption
- No new FDA approved therapies for gastroparesis since 1980

Ready-made Market

- 4M prescriptions of oral metoclopramide annually
- 20-50% of patients use off-label treatments or go untreated

Potential for Premium Pricing

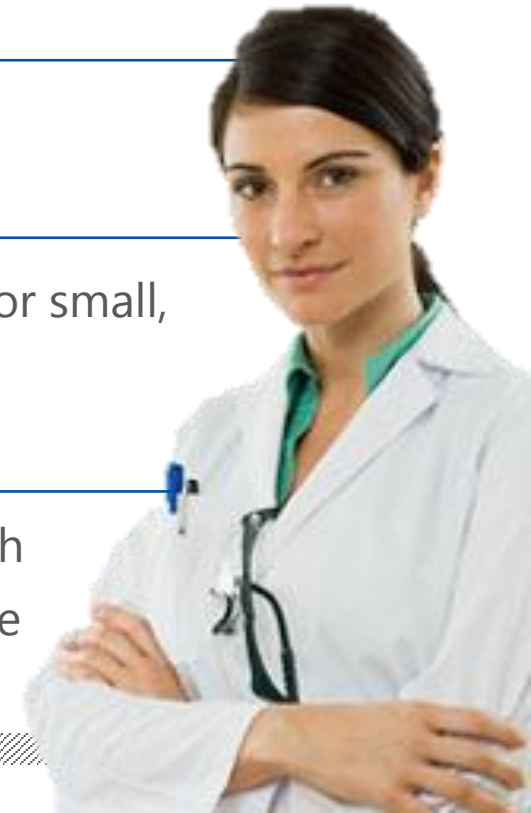
- 30 national and regional plans indicate limited reimbursement impediments based upon various pricing scenarios

Appropriate for Specialty Salesforce

- ~7,200 metoclopramide prescribing gastroenterologists allows for small, targeted salesforce
- Significant referrals for diagnosis/treatment from specialists

Rapid Uptake Possible

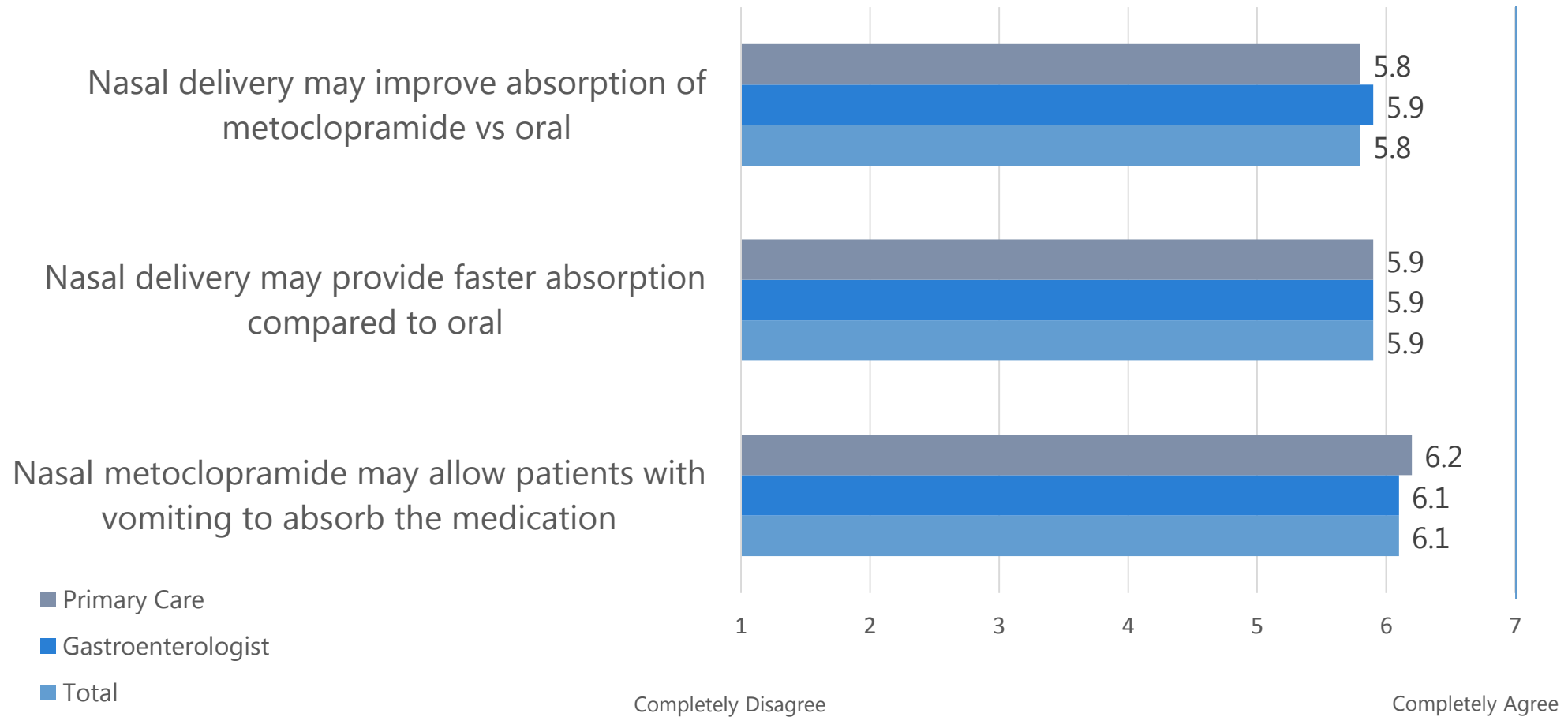
- No expected competitive sales force for several years after launch
- Market research shows rapid incorporation into treatment regime



Current Competitive Landscape

Product	Class	Route	Company	Development Status
Gimoti	Dopamine antagonist & mixed 5-HT₃ antagonist/ 5-HT₄ agonist	Nasal	Evoke Pharma	505(b)(2) NDA submitted June 2018 Positive comparative exposure PK study results and discovery of sex-based differences Phase 3 (n=205): Statistical significance achieved in women with moderate to severe gastroparesis symptoms at baseline. Did not meet primary endpoint for ITT.
Relamorelin	Ghrelin agonist	Sub Cutaneous	Allergan	Phase 3 (enrolling) results expected in 2020 Phase 2b results: Failed to meet primary endpoint in symptomatic relief of vomiting reduction. Phase 2a results: Failed to meet secondary symptom endpoint with either dose
Velusetrag	5-HT ₄ agonist	Oral	Takeda/ Theravance	Phase 2b (n = 232) Mixed results with three doses (5, 15, and 30 mg). No dose response. More side effects with higher doses. Phase 2a (n=34) results: No results reported for symptom relief
Tradipitant	NK-1 antagonist	Oral	Vanda	Phase 2 (enrolling): No prior results in gastroparesis
Renzapride	5-HT ₄ agonist and 5HT-3 antagonist	Oral	EndoLogic	Phase 2a (completed 2008): No results reported for symptom relief (gastric emptying only)
ATC-1906	D2/D3 receptor antagonist	Oral	Takeda	Phase 1 (ongoing): No known results
NG-101	D2/D3 receptor antagonist	Oral	Neurogastrx	Phase 1: No gastroparesis results

Mode of Delivery Attributes

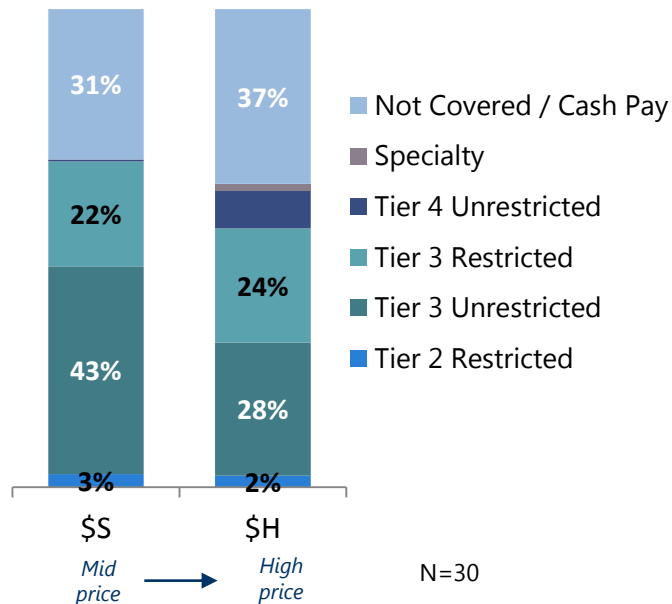


Source: ZS Associates Gastroparesis quantitative survey (n=121), Question 4Q5: How much do you agree with each of the following statements?
Totals weighted based on average metoclopramide TRx's per high/medium segment

Anticipate Gimoti to be widely available to commercial plan members

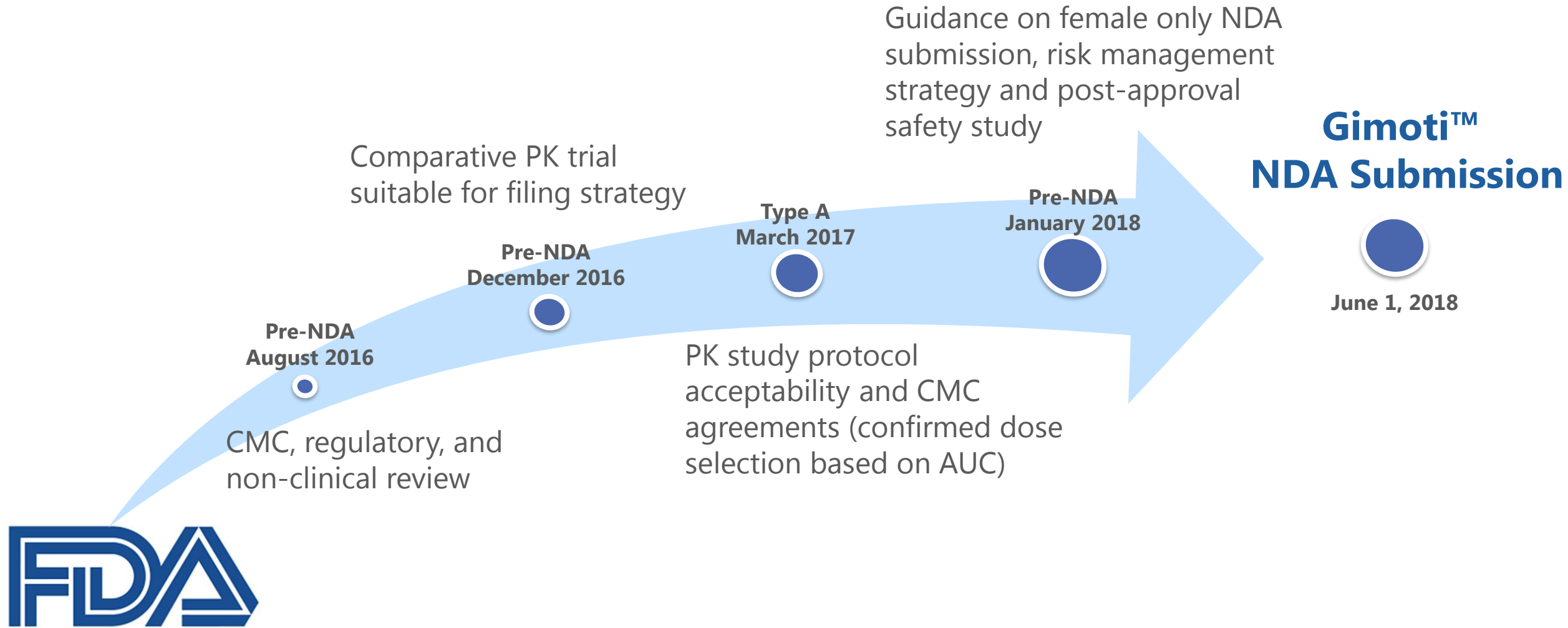
Management of Gimoti at Evaluated Prices
(Coverage by Percentage of Lives)

Gimoti benefit vs. standard of care



- Mostly Tier 3 “Unrestricted” or “Restricted” coverage projected (typical for branded products)
 - Typical co-pay for most branded products
 - Little difference in coverage at similar (\$S) or high (\$H) price to current branded GI products
- Similar reimbursement regardless of label differentiation
- Ample commercial insurance reimbursement expected due to:
 - Lack of competitive products
 - Large unmet need
 - Significant current medical costs for hospitalization

Source: Campbell Alliance Web-based surveys with 18 pharmacy directors and 12 medical directors. April 29 through May 26, 2015.



Objective: Identify a Gimoti dose with systemic exposure equivalent to Reglan Tablets (the reference listed drug)

- A 4-period, 4-treatment, 4-sequence randomized crossover study of the bioavailability and PK of Gimoti and Reglan Tablets
- ~100 male & female healthy volunteers for PK analysis, 90% power
- Doses
 - 3 Gimoti strengths
 - Reglan Tablets 10 mg

Results

- Gimoti dose achieved equivalent exposure for AUC
 - Previously discussed with FDA dose selection based on AUC = between 80%-125%
- C_{max} was slightly lower than the RLD
 - Results anticipated for different route of administration and discussed with FDA prior to trial
 - Reference: 21 CFR Part 320.23 Bioavailability and Bioequivalence Requirements allow for variations in rate of absorption (C_{max})



- Exposure differences in women and men given same metoclopramide dose
 - Statistically significantly lower AUCs in men
 - Not attributable to body mass index (BMI) or weight
 - Regardless of the route of administration (nasal, oral, IV)
- PK differences may explain sex-specific efficacy results
 - Gimoti reduced symptoms of gastroparesis in women, but not men
- Female-only NDA filed June 1, 2018
 - Equivalent exposure to Reglan Tablets
- Patents filed
 - Dosing by sex (Comparative PK data)
 - Efficacy by sex (Differential efficacy Phase 2 & 3)
 - Granted in EU and Mexico thus far



- Manufacturing
 - Considerable Chemistry, Manufacturing & Controls data developed to date
 - Ongoing stability testing (3 years stability from prior batches)
 - Commercial manufacturing agreement announced with Patheon (ThermoFisher)
- Distribution
 - Currently evaluating firms for commercial relationship
 - Targeting wholesale and pharmacy providers for beneficial partnering
- Marketing & Sales
 - Ongoing relationship with Syneos Health (formerly inVentiv Health) for marketing sales and other commercial capabilities
 - Capabilities for multiple aspects of commercial infrastructure



- Current patents provide protection against:
 - Delivering metoclopramide into the nose to treat symptoms associated with gastroparesis; and
 - Using a spectrum of stable liquid formulations containing metoclopramide
- Granted gender specific patents in the European Union and Mexico with coverage until 2032

U.S. Granted Patents

Patent #	U.S. 6,770,262	U.S. 8,334,281
Title	Nasal Administration of Agents for the Treatment of Gastroparesis	Nasal Formulations of Metoclopramide
Expires	2021	2030

PCT Application

Application #	PCT/US2012/052096
Title	Treatment of Symptoms Associated with Female Gastroparesis
Expires	2032 (if granted)

Event	Timeline	Completed
Topline comparative exposure PK data	Q4, 2017	✓
Pre-NDA meeting with FDA	Q1, 2018	✓
NDA submission	Q2, 2018	✓
NDA acceptance	Q3, 2018	
PDUFA goal date	H1, 2019	

\$2.4M PDUFA fee waiver granted for Gimoti NDA
Cash runway extended into April 2019

Income Statement Data (in USD)

1Q 2018	(Ended March 31, 2018)
Operating Expenses	
Research & Development	\$1.4M
General Administrative	\$1.0M
Total Operating Expense	\$2.4M
Other (Income) Expense	(\$0.4M)
Net Loss	\$2.0M

Cash (in USD) and Equity Data

	March 31, 2018
Cash Balance	\$5.4M
Common Shares Outstanding	15.7M
Warrants	2.8M
Stock Options	2.8M

- **Gimoti™**: novel nasal delivery of metoclopramide for the symptomatic relief of acute and recurrent diabetic gastroparesis in women
- **Serves unmet clinical need**: Provides predictable absorption despite gastroparesis symptoms or stomach emptying status; bypasses the GI tract
- **Large market opportunity**: ~12-16M patients with symptoms (80% women); ~2-3M currently treated in US given limited efficacy from few available treatment options
- **Only one FDA-approved therapy for gastroparesis**: Metoclopramide (oral & IV) still has ~4M million prescriptions of the oral medication prescribed annually
- **Positive data from pivotal comparative exposure PK study**: Gimoti demonstrated AUC equivalence
- **Female only 505(b)(2) NDA**: Submitted June 1, 2018