TARGACEPT Building Health, Restoring Independence®


# Jefferies 2014 Global Healthcare Conference

June 3, 2014

# Cautionary Note: Forward-Looking Statements

This presentation includes “forward-looking statements” made under the provisions of the Private Securities Litigation Reform Act of 1995. Forward-looking statements include statements, other than statements of historical fact, regarding, without limitation: the progress or scope of development of TC-5214, TC-1734, TC-6499, AZD1446 or any other Targacept product candidate, such as the target indication(s) for development, the size, design, population, conduct, duration or objective of any clinical trial or the timing for initiation or completion of any clinical trial, for availability of results from any clinical trial or for submission or approval of any regulatory filing; the competitive position of any Targacept product candidate or the commercial opportunity in any indication; any payments that AstraZeneca may make to us; or our plans, expectations, objectives, prospects or future operations, financial position, revenues, costs or expenses. The words “may,” “will,” “could,” “would,” “should,” “expect,” “intend,” “plan,” “anticipate,” “believe,” “estimate,” “predict,” “project,” “forecast,” “potential,” ““continue,” “ongoing,” “scheduled” and similar expressions are intended to identify forward-looking statements. Actual results, performance or experience may differ materially from those expressed or implied by any forward-looking statement as a result of various important factors, including our critical accounting policies and risks and uncertainties relating without limitation to: whether findings from nonclinical studies and assessments of TC-5214 and clinical trials of TC-5214 in a different indication will be predictive of a positive outcome in our ongoing Phase 2b clinical trial of TC-5214 in overactive bladder; and the control or significant influence that AstraZeneca has over the development of AZD1446, including as to whether to conduct further development. Risks and uncertainties that we face are described in greater detail under the heading “Risk Factors” in our most recent Annual Report on Form 10-K and in other filings that we make with the Securities and Exchange Commission. As a result of the risks and uncertainties to which our business is subject, the results or events indicated by the forward-looking statements may not occur. In addition, market and industry statistics contained in this presentation are based on information available to us that we believe to be reliable but have not independently verified.

All forward-looking statements speak only as of the date this presentation is made and should not be relied upon as representing our views as of any date after this presentation is made. We specifically disclaim any obligation to update any forward-looking statement, except as required by applicable law.

# Targacept: Positioned for Success

- **Diverse clinical pipeline**
  - Phase 2b study of TC-5214 in overactive bladder fully recruited; top-line results expected in mid 2014
    - Strong mechanistic rationale, objective endpoints and large unmet need
  - Phase 2b Alzheimer's disease study with NNR modulator targeting α4β2 (TC-1734) fully recruited; top-line results expected in mid 2014
  - Additional α4β2 modulator (AZD 1446) licensed to AstraZeneca
  - Preparing for exploratory clinical study of TC-6499 in diabetic gastroparesis
- **Platform built on uniquely diverse class of therapeutic targets, with a history of attracting significant alliances**
- **Strong balance sheet and track record of capital efficiency**

# Clinical-Stage Pipeline Focused on Large Unmet Medical Needs

| | | NNR Subtype | Preclinical | Phase 1 | Phase 2 | Phase 3 | |
|---|---|---|---|---|---|---|---|
| Overactive Bladder | TC-5214 | α3β4 | → | → | → | | |
| Alzheimer's Disease | TC-1734 | α4β2 | → | → | → | | |
| Diabetic Gastroparesis[1] | TC-6499 | α3β4 / α3β2 | → | → | → | | |
| TBD | AZD1446/TC-6683 | α4β2 | → | → | → | | AstraZeneca |

[1] *Expected to initiate in mid-2014*





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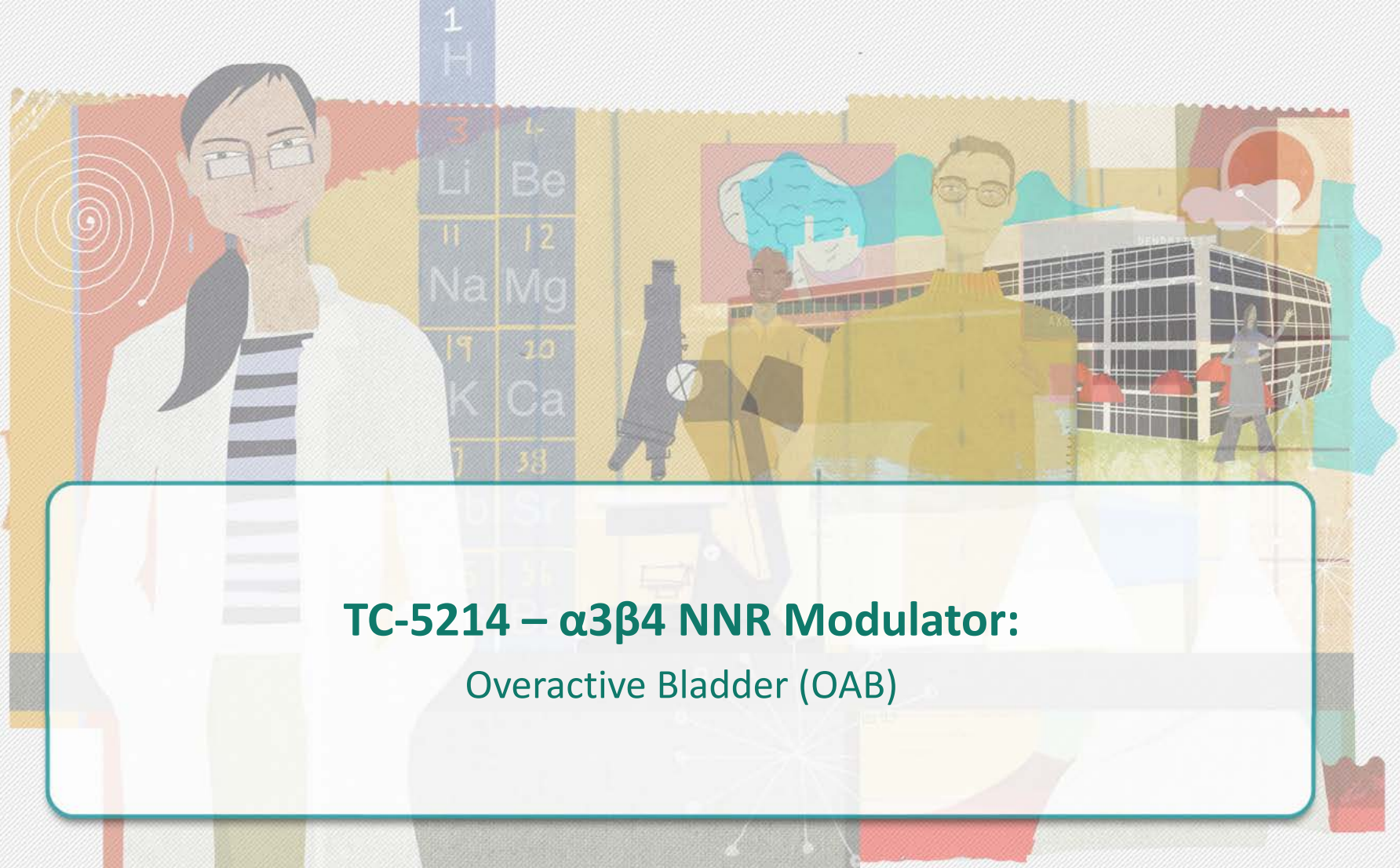

# TC-5214 – α3β4 NNR Modulator:

## Overactive Bladder (OAB)





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# TC-5214: Opportunity in OAB

- **Approximately 1 in 6 US adults are estimated to suffer from OAB[1]**
  - Reduced quality of life due to decreased ability to socialize and participate in life activities, sleep disturbances and decreased emotional well-being
  - Patients/doctors searching for novel agents with greater efficacy/fewer side effects
- **Historically, an indication where Phase 2 success has consistently translated to Phase 3 success and approval**
- **Substantial commercial opportunity (OAB drugs ≈ $3.5 Billion[2])**

[1]Stewart WF, Van Rooyen JB, Cundiff GW, Abrams P, Herzog AR, Corey R, et al. Prevalence and burden of overactive bladder in the United States. *World J Urol*. May 2003;20(6):327-36.
[2]Decision Resources *Decision Base 2011 Overactive Bladder: Will Advantages in Tolerability Be Sufficient to Give Emerging Agents an Edge Over Currently Marketed Anticholinergics?*

# Overactive Bladder: Commercial Landscape

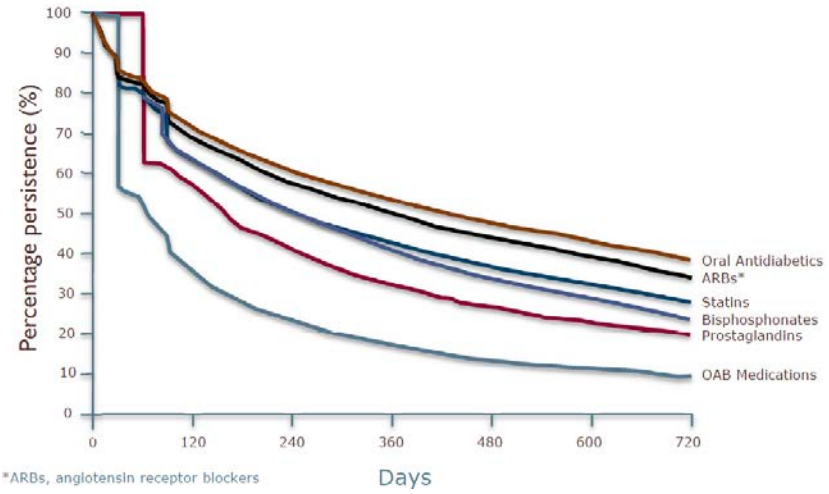
- **Muscarinic antagonist drugs are the current standard of care for treatment of OAB**
- **Recent approvals of beta-3 adrenergic agonist (Myrbetriq$^{R}$) and label expansion for Botox® in refractory patients provide alternative therapies**

| | Muscarinic Antagonists | Beta-3 Adrenergic Agonist | Botulinum Toxin |
|---|---|---|---|
| **Major Brands / Products** | VESIcare (solifenacin succinate); Toviaz (fesoterodine fumarate); DITROPAN (oxybutynin chloride); SANCTURA XR (trospium chloride extended release capsules); Detrol (tolterodine tartrate) | Myrbetriq (mirabegron) extended-release tablets 25 mg/50 mg | BOTOX onabotulinumtoxinA |
| **Efficacy** | ~0.5 – 1.0 micturitions | ~0.4 micturitions | ~1.0 – 1.7 micturitions/day |
| **Safety/Tolerability** | Dry mouth 20-60% | CV, liver, skin | UTI, urinary retention |
| **Administration** | Oral (QD or BID) | Oral (QD) | 20 injections directly into bladder (every ~6 months) |
| **WW Sales (2011)** | <$3+ billion (Vesicare leading brand at $1.0+ billion) | Unknown (launched 4Q12) | Unknown (idiopathic OAB approval 1Q13) |
| **Generic** | Some now and all by 2018/2019 | Unknown but 2023 latest | Unknown |

# Overactive Bladder: Significant Growth Opportunity for an Effective, Safe and Well-Tolerated Product

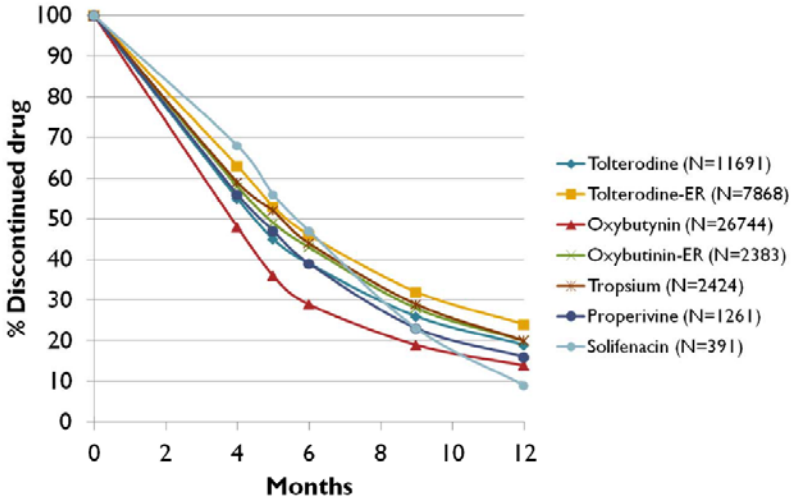
- **Due to poor tolerability, patient persistence and compliance is low with OAB products…yet still greater than a $3 billion market**

## Time to drug discontinuation in six chronic therapy classes




Yeaw J et al. J Manag Care Pharm. 2009;15:728–40

## Antimuscarinic Therapy of OAB Time to Discontinuation - US




Gopal et al, Obstetrics and Gynecology 112:(6) December 2008

- **TC-5214 has to date demonstrated a favorable safety and tolerability profile**
- **Very few compounds are in development and none that are known to have a novel mechanism**

# TC-5214: Strong Mechanistic Rationale for Development in OAB

- **Oral agent targets drug delivery into the bladder**
  - >90% of administered dose is eliminated unchanged through bladder
  - Low dose to produce high bladder concentrations that could diminish sensation of urgency and be well tolerated
- **Potent nicotinic activity in the bladder**
  - Blocking nicotinic receptors in bladder shown preclinically to decrease bladder wall contraction frequency and impact nerve signaling
- **Physiological findings from TC-5214 Major Depressive Disorder program and additional preclinical outcomes consistent with marketed treatments for OAB**

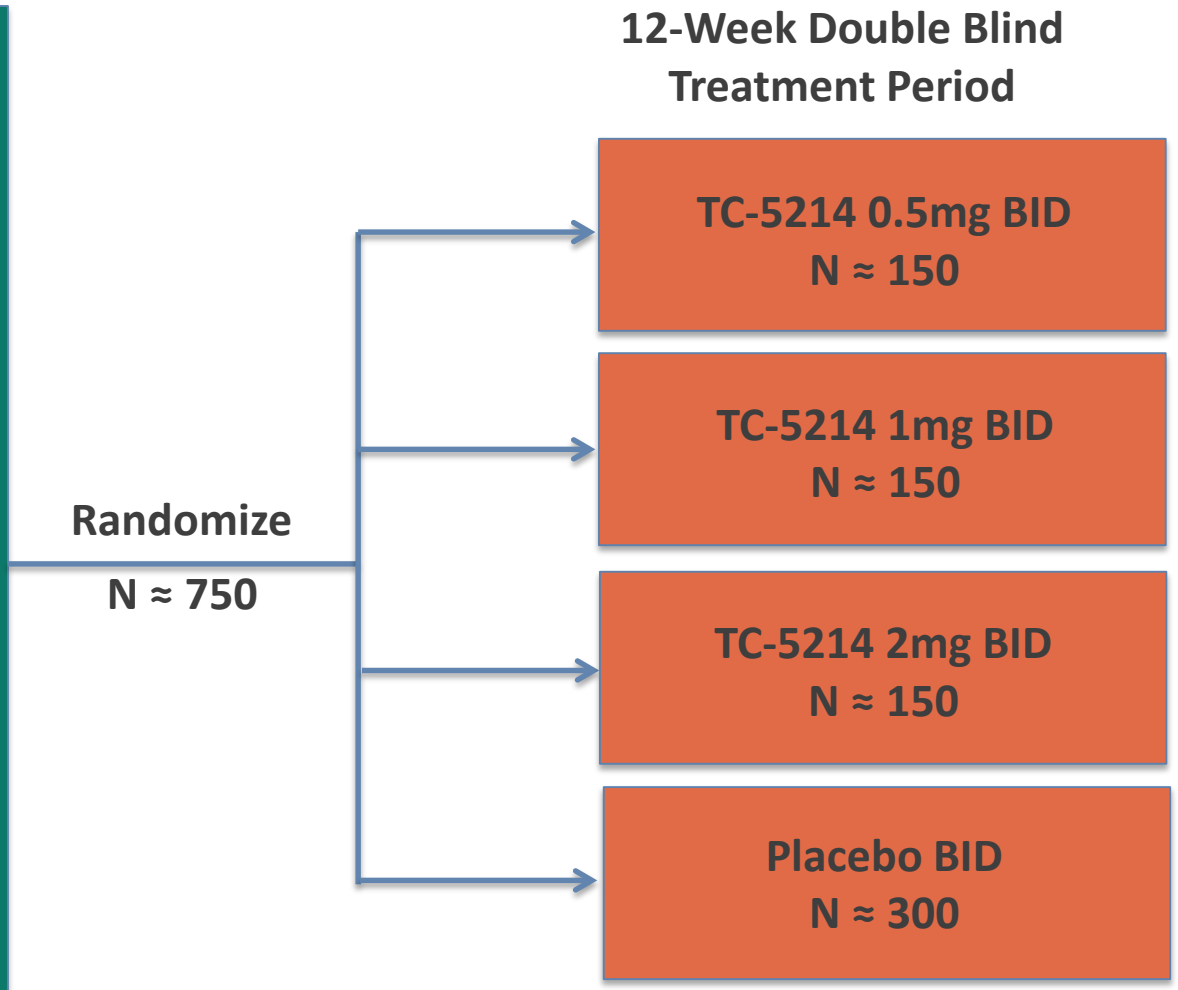
# TC-5214: Design of Ongoing Phase 2b Trial in OAB

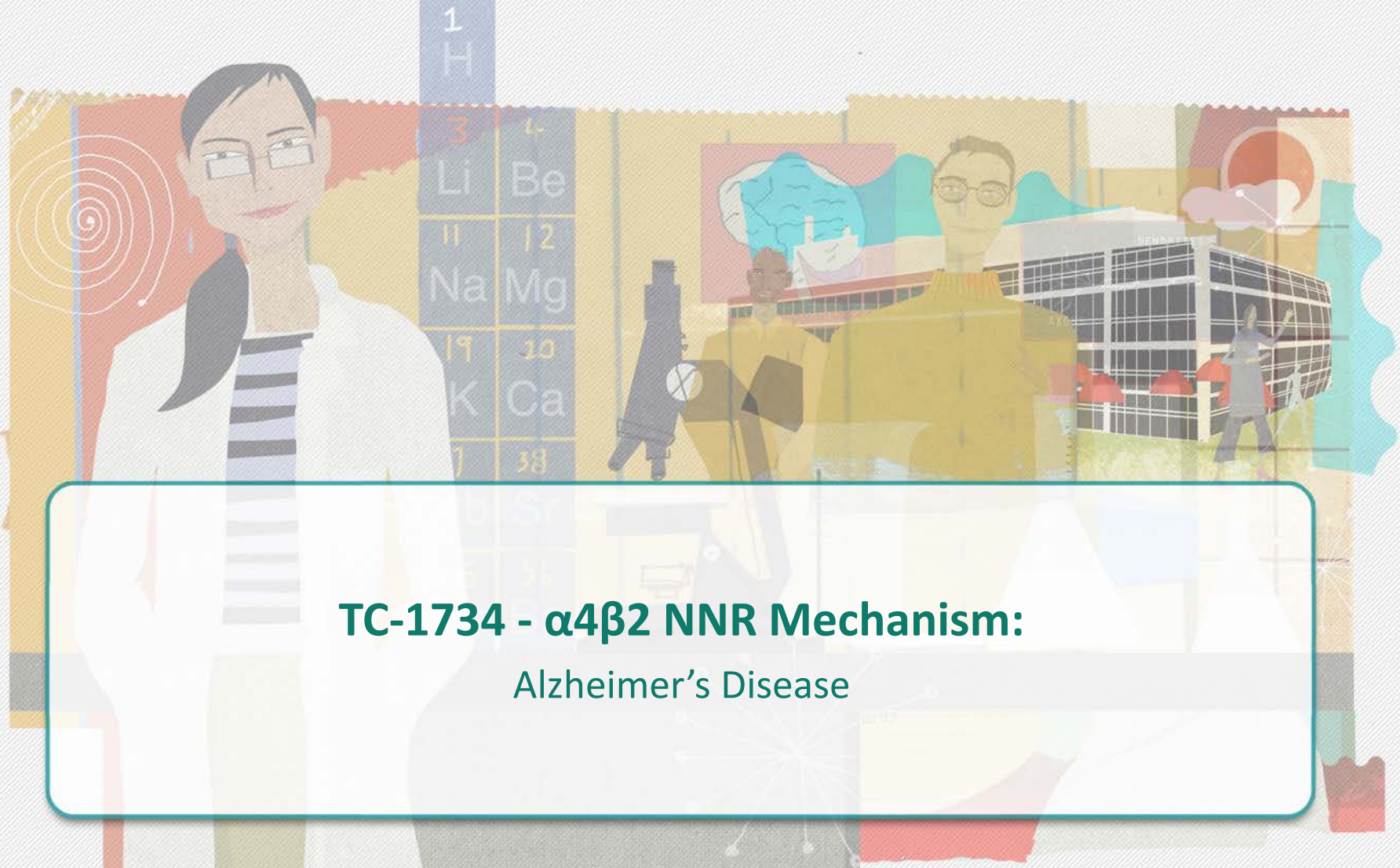
**Co-Primary Endpoints:**

- Change in micturition frequency per 24 hours (baseline vs. week 12)
- Change in urinary incontinence episodes per 24 hours (baseline vs. week 12)

**Additional Information:**

- 3-5 week screening period
- 2 week follow-up period
- ~ 130 U.S. sites





# TC-1734 - α4β2 NNR Mechanism:

## Alzheimer's Disease





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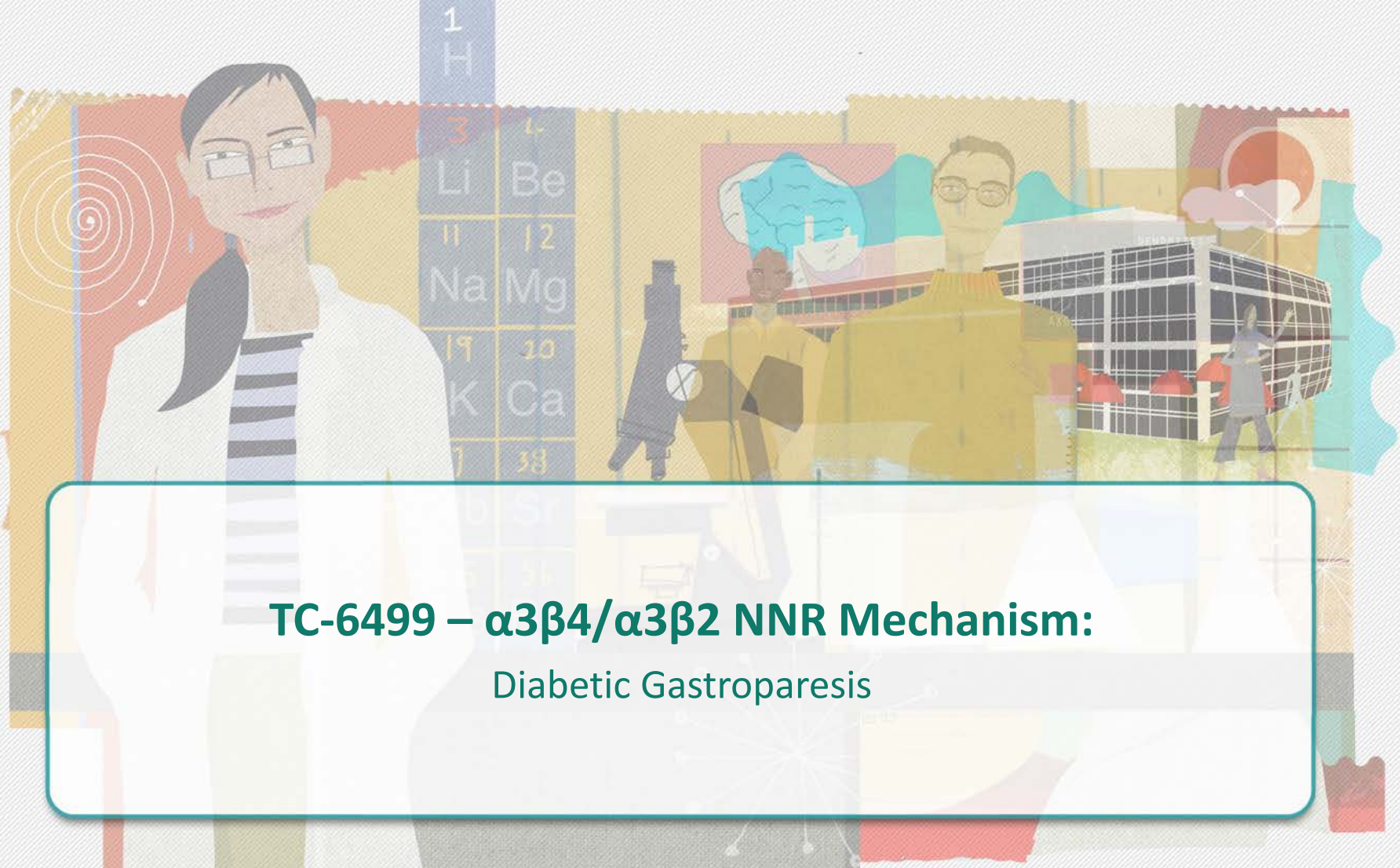
# TC-1734: An α4β2 NNR Modulator in a Phase 2b Alzheimer's Disease Study

- **Previously studied in 1,350 subjects in various cognitive disorders**
- **FDA's Special Protocol Assessment process utilized to confirm Phase 2b study as potential registration trial**
- **Randomized, double blind trial at predominantly Eastern European and some US sites**
  - Once-a-day dosing over 12-month treatment period
  - Designed to randomize approximately 300 patients with mild to moderate Alzheimer's disease; recruitment completed
  - Head-to-head design – 30mg TC-1734 vs. donepezil
- **Primary outcome measures**
  - Alzheimer's Disease Assessment Scale-cognitive subscale (ADAS-Cog) and Clinician's Interview Based Impression of Change (CIBC-(+)) (US)
  - ADAS-Cog and Alzheimer's Disease Cooperative Study Activities of Daily Living (ADCS-ADL) (Europe)



# TC-6499 – α3β4/α3β2 NNR Mechanism:

## Diabetic Gastroparesis





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# TC-6499 and Diabetic Gastroparesis

- Gastroparesis (GP) is a large unmet medical need[1]
  - GP is a chronic disorder whereby muscles in the stomach don't function normally which slows or stops the movement of food from the stomach to the small intestine
  - Diabetes is the most common known cause. GP is estimated to affect 2.2 million diabetics in the U.S. and can result in recurrent hospitalizations
- TC-6499 achieved proof-of-principle in:
  - Phase 1 by increasing both gastric and intestinal motility
  - Phase 2a by significantly increasing spontaneous bowel movements in IBS-constipated patients
- TC-6499 represents a novel and potentially preferential mechanism of action
- Potential suitability for chronic use differentiates TC-6499 from current treatments
- Plan to conduct an exploratory crossover design clinical trial (n~18) evaluating 3 doses of TC-6499 and placebo in diabetic GP subjects utilizing carbon 13 breath test as a surrogate measure of gastric motility.
  - Trial expected to initiate in mid 2014

*1 References on file*





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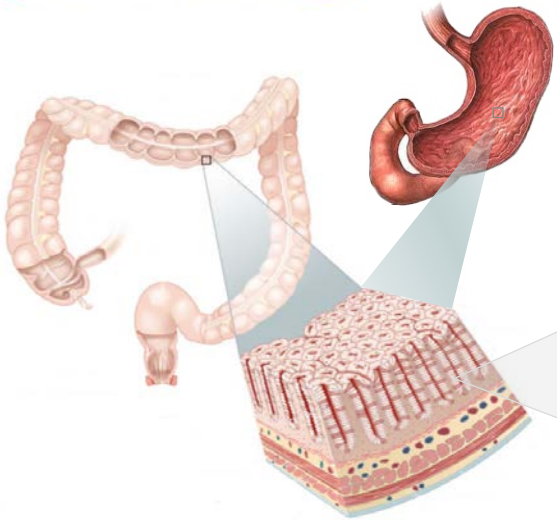
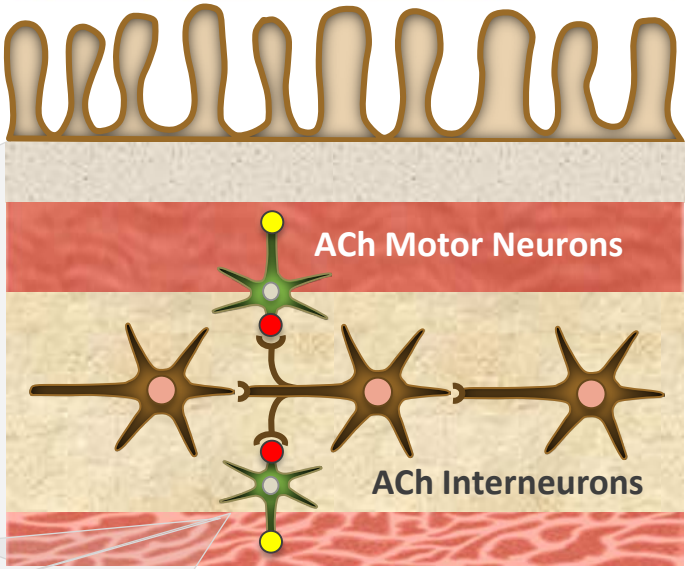
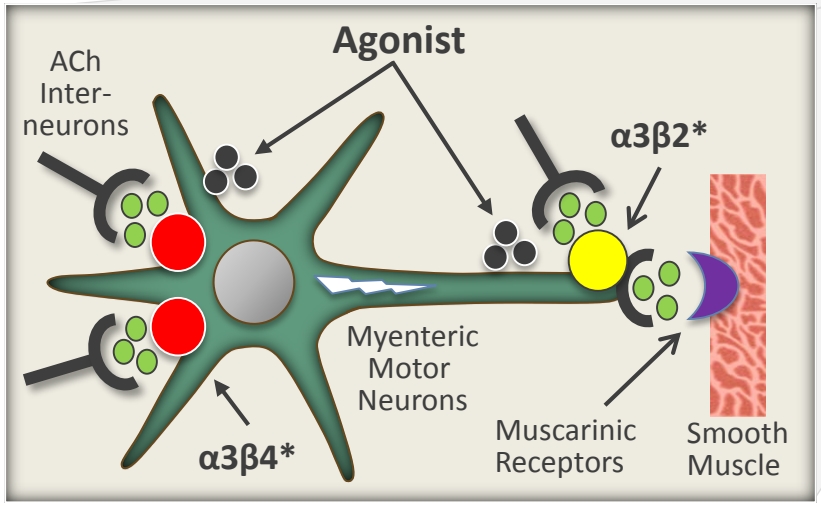
# Locally Acting α3* Agonists for Hypo-Motility Disorders: Proposed Mechanism of Action






- Post-synaptic **α3β4*** activation increases motor neuron firing
- **α3β2*** amplifies ACh release from motor neurons to activate muscarinic receptors on smooth muscle cells and stimulate peristalsis





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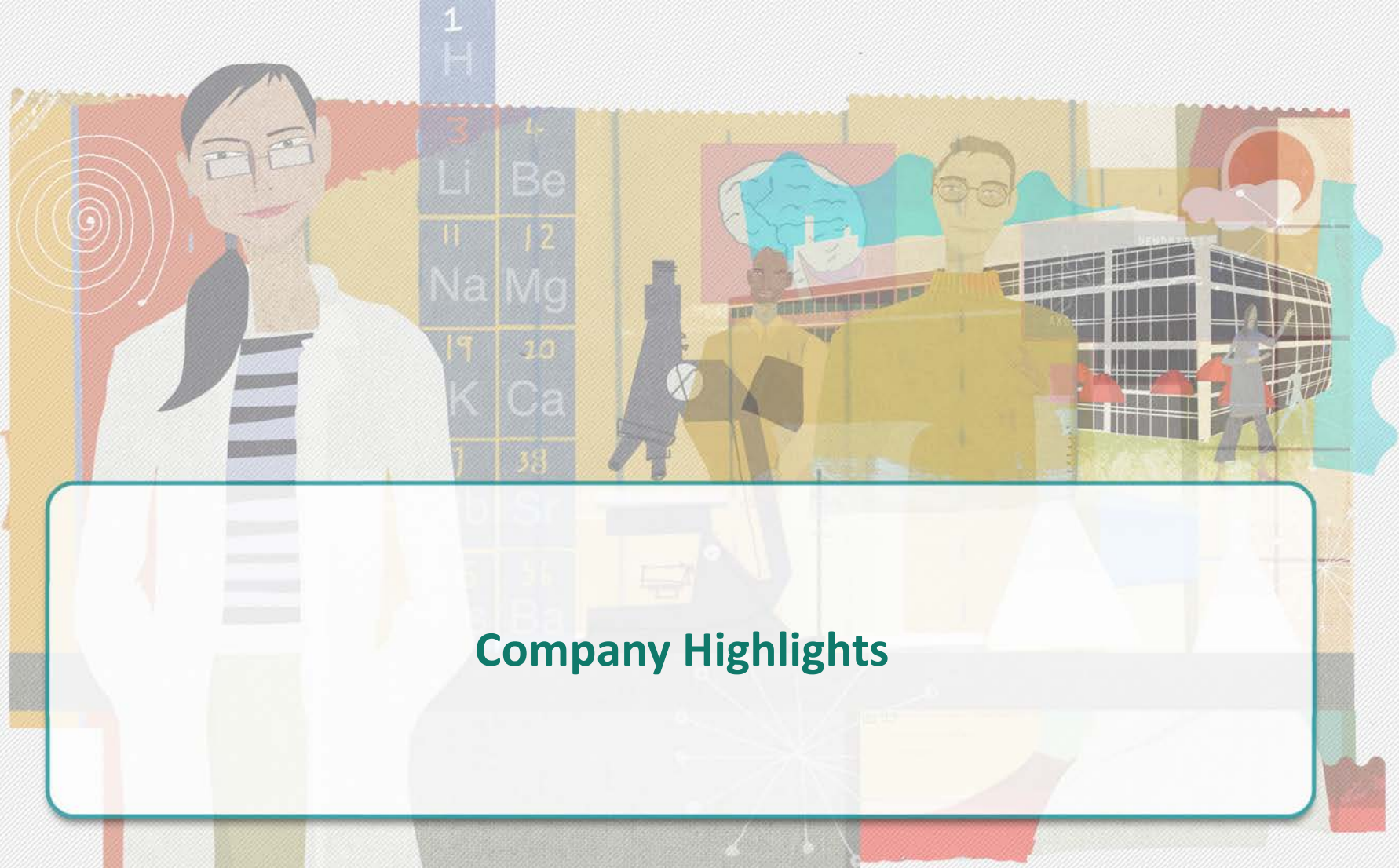

# Company Highlights

# Financial Highlights

(All Information in Thousands)

| Operating Statement | Three Months Ended 3/31/2014 | Year Ended 12/31/2013 |
|---|---|---|
| Operating Revenues | $87 | $3,629 |
| R&D Expense | 9,080 | 38,840 |
| G&A Expense | 2,763 | 12,005 |
| Net Loss before Income Taxes | ($11,587) | ($46,705) |
| **Cash Position & Capitalization** | **3/31/14** | **12/31/13** |
| Cash and Investments | $132,143 | $143,777 |
| Total Debt | 918 | 1,136 |
| Shares Outstanding | 33,785 | 33,718 |





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# Anticipated Key Events

| | | |
|---|---|---|
| **TC-5214** | α3β4 NNR Modulator | • Recruitment completed for Phase 2b study in overactive bladder; top-line results expected mid-2014 |
| **TC-1734** | α4β2 NNR Modulator | • Recruitment completed for Phase 2b study in Alzheimer's disease; top-line results expected mid-2014 |
| **AZD1446** | α4β2 NNR Modulator | • Determine with AstraZeneca target indication for further development |
| **TC-6499** | α3β4 / α3β2 NNR Modulator | • Conduct an exploratory clinical study of TC-6499 in diabetic gastroparesis |

**Diverse Pipeline and Strong Balance Sheet Diversify Risk**

# Targacept: Positioned for Success

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