Forward Looking Statements

This presentation contains "forward-looking statements." These statements include words like "may," "expects," "believes," “plans,” “scheduled,” and "intends," and describe opinions about future events. These forward-looking statements involve known and unknown risks and uncertainties that may cause the actual results, performance or achievements of BioLineRx to be materially different from any future results, performance or achievements expressed or implied by such forward-looking statements.
BL-7040: Novel Oligonucleotide for IBD

- **Indication**: Inflammatory bowel disease (IBD)
- **Mode of Action**: Toll-Like Receptor 9 (TLR-9) agonist
- **Status**: Phase II clinical trial in progress
- **Product Highlights**:
  - Orally available synthetic oligodeoxynucleotide (2\textsuperscript{nd} generation)
  - Oligo sequence was chemically modified (2’OMe) to increase stability
  - Safety and tolerability demonstrated in clinical trials
  - Efficacy demonstrated in animal models of IBD
    - Comparable to dexamethasone
- **Market opportunity**: ~$8 billion in 2012 (Datamonitor)
- **Intellectual Property**: Patent applications granted or filed worldwide, valid through 2024 (not including extension)
IBD Overview

• A group of inflammatory conditions of the colon and small intestine

• Two major types:
  – Ulcerative Colitis (UC): limited to the colon
  – Crohn’s Disease (CD): involves multiple segments of the gastrointestinal tract

• Common end pathway for both types consists of inflammation of mucosal lining of intestinal tract
  – Causes ulceration, edema, bleeding, and fluid and electrolyte loss

• ~2.6 million people affected by IBD (1.7M UC; 0.9M Crohn’s) across seven major markets in 2011 (Datamonitor)
  – Expected to reach 2.9 million by 2019
BL-7040: Background and Rationale

• Synthetic 20 base oligonucleotide

• Previously developed for Myasthenia Gravis (MG), an autoimmune neuromuscular disease
  – Demonstrated safety and efficacy in humans

• BioLineRx has designated BL-7040 for inflammatory diseases
  – BL-7040 ameliorates inflammation through modulation of AChE and TLR-9

• Toll-Like Receptor 9 (TLR-9)
  – TLRs are key pattern recognition receptors of the innate immune system
  – TLR-9 is expressed throughout the whole GI tract
  – TLR-9 activation causes anti-inflammatory reaction
  – TLR-9 agonists can prevent acute inflammatory flares in intestinal mucosa
BL-7040’s Specificity Towards TLR-9 Demonstrated In-Vitro

- Specificity of BL-7040 to TLR-9 was assessed via Luciferase reporter quantification of NFkB activation in HEK-293 cells stably transfected with various TLR’s
  - For the HEK293-TLR 2,3,4,5,7,8 and 9 the known ligands were PAM2, Poly I:C, LPS K12, Flagellin, R848, R848, and CpG-B (ODN 1826), respectively
  - Luciferase reporter quantification of NFkB activation in HEK-293 cell lines stably expressing specific TLR proteins and treated with BL-7040 (100µM)
    - HEK-293 cells expressing the reporter gene alone (TLR-) were used as a negative control

Gilboa-Geffen et al. (2011) PLoS ONE 6(12)
**Pre-Clinical Efficacy Data**

BL-7040 is as Effective as Dexamethasone in Treating Established IBD

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**Study design:**

1. Colitis induced in Balb/c mice using TNBS
2. Mice were administered BL-7040 orally for 7 days, starting 24h or 48h post colitis induction (Left)
3. Disease severity was assessed using the Wallach score
4. Reduced cytokine (Right) induction in intestinal explants pretreated for 24hr with BL-7040 (1μM) and then treated with 1μg/ml LPS for another 24hr
Pre-Clinical Safety Highlights

• No adverse effect on respiratory or central nervous system (CNS) following oral or intravenous administration

• No treatment-related changes in electrophysiological parameters following daily repeated administration of BL-7040 to monkeys

• No evidence of mutagenic activity

• Repeated oral administration of BL-7040 to rats and monkeys at 1000 mg/kg/day was well tolerated
  • No treatment related clinical signs, no effect on overall bodyweight gain, food consumption, hematology, blood chemistry or urinalysis parameters.
  • No macroscopic changes or effect on organ weights

• Daily doses utilized in repeated-dose toxicology studies in primates and rats were significantly higher (484 and 242 times higher, respectively) than highest doses proposed for human studies
Bench to Bedside to Partner

BIOLINE RX