

## BEST-IN-CLASS, BROAD-SPECTRUM FLUOROQUINOLONE WITH POTENT MRSA COVERAGE

### Potent MRSA Activity And Low Propensity For Development Of Drug Resistance

- ◆ Phase III ready, novel broad-spectrum fluoroquinolone (FQ) antibiotic with potent activity against MRSA
- ◆ Positive Phase II POC study for ABSSSI indication
- ◆ Highly differentiated from marketed quinolones: covers common, difficult-to-treat pathogens
- ◆ Low propensity for development of drug resistance
- ◆ IV and oral formulations enable step-down Rx
- ◆ Favorable safety profile
- ◆ Community acquired pneumonia study in progress (IV to oral switch)
- ◆ Excellent lung penetration in humans

### Positive Phase II Results For Acute Bacterial Skin And Skin Structure Infections (ABSSSI)

Phase II POC study was conducted using non inferiority design (based on FDA 2010 Guidance for ABSSSI) 161 patients: 250 mg JNJQ2 BID vs. Linezolid 600 mg BID (7-14 d)

- ◆ JNJ-Q2 was non-inferior based on new FDA draft guidance endpoint: 61.4% JNJ-Q2 vs. 57.7% linezolid treated patients had lack of spread of lesion + absence of fever at 48-72h
- ◆ Favorable safety profile. Nausea and vomiting, which were mostly mild and self limiting, were the most common AEs

Treatment Days	% of Patients Cured	
	JNJ-Q2	Linezolid
7 days	44.6%	37.2%
10-14 days	66.3%	61.5%
2-14 days post Rx	83.1%	82.1%

Success (non-inferiority) at all clinical cure (secondary) endpoints with trend toward more rapid cure with JNJ-Q2

### Development Status

- ◆ Significant number of subjects (N~330) have been dosed in clinical trials (Phase I and Phase II)
- ◆ Phase II POC study in ABSSSI (complicated skin and soft tissue infections) complete: non-inferiority vs. linezolid. Community acquired pneumonia study in progress ®
- ◆ Eight Phase I studies completed, including QT study and human bioavailability studies
- ◆ Potential for NDA submission 2014; no rate limiting preclinical studies for NDA

### Clinical Doses Expected To Cover Diverse Pathogens, Multiple Indications:

#### Gram +

- ✓ Staph aureus: including MRSA (FQ, vanco, linezolid, dapto resistant)
- ✓ Strep pneumoniae: including MDR and other strep
- ✓ Enterococcus
- ✓ Staph epidermidis



#### Gram -

- ✓ H flu
- ✓ Moraxella
- ✓ E coli (cipro sens and intermediate)
- ✓ Enterobacter species
- ✓ Klebsiella pneumoniae
- ✓ Proteus mirabilis
- ✓ N. gonorrhoeae (including cipro resistant)



#### Atypical Bacteria

- ✓ Legionella
- ✓ Chlamydia
- ✓ Mycoplasma



#### Anaerobes

- ✓ Gm+
- ✓ Gm- (including Bacteroides fragilis)

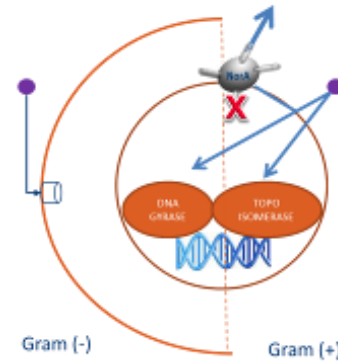


**JNJ-Q2 is Highly Potent Against Resistant Staph aureus, With Low Propensity For Drug Resistance**

Organism	No. of Isolates	Compound	MIC in µg/mL	
			MIC Range	MIC <sub>90</sub>
Staph aureus (All Isolates)	511	JNJ-332729463	≤0.008 - 4	0.5
	511	Levofloxacin	0.12 - >16	>16
	511	Linezolid	0.5 - 4	2
	511	Vancomycin	0.5 - 2	1
Fluoroquinolone resistant - methicillin resistant - S. aureus	308	JNJ-332729463	0.12 - 4	1*
	308	Levofloxacin	4 - >16	>16
	308	Linezolid	0.5 - 4	2
	308	Vancomycin	0.5 - 2	1
Fluoroquinolone susceptible - methicillin resistant - S. aureus	50	JNJ-332729463	≤0.008 - 0.015	≤0.008
	50	Levofloxacin	0.12 - 0.5	0.25
	50	Linezolid	1 - 2	2
	50	Vancomycin	0.5 - 1	1
Fluoroquinolone resistant - methicillin susceptible - S. aureus	101	JNJ-332729463	0.12 - 2	0.5
	101	Levofloxacin	4 - >16	>16
	101	Linezolid	1 - 2	2
	101	Vancomycin	0.5 - 2	1
Fluoroquinolone susceptible - methicillin susceptible - S.	52	JNJ-332729463	≤0.008 - 0.015	0.015
	52	Levofloxacin	0.12 - 0.5	0.25
	52	Linezolid	1 - 2	2
	52	Vancomycin	0.5 - 2	1

\* 97% of isolates covered at ≤1 µg/mL; 95% EU isolates ≤0.5 µg/mL; 87% US isolates ≤0.5 µg/mL.

- ◆ Equipotent inhibition of two key bacterial targets protects against resistance
- ◆ NOT a substrate for known FQ efflux pumps
- ◆ 4-180-fold more potent vs comparator FQs
- ◆ More potent and more active than the other FQs and vanco against biofilms of MSSA and MRSA
- ◆ In serial passage, more time needed to generate MRSA mutants resistant to JNJ-Q2 (33+ days) vs. cipro (9 days).
  - ◆ For JNJ-Q2, resistance occurred after 9 mutations
  - ◆ In contrast, cipro resistance occurred with only 2 mutations



**Significant Potential For a Variety of Unmet Needs in Growing Markets**

**JNJ-Q2 Has Significant Potential In Both Markets**

**\$6 B Fluoroquinolone Market**

Market Drivers

- Familiar class
- Broad spectrums
- Potency
- Oral & IV formulation
- Shorter course
- Multi-indications
- Emerging resistance in respiratory pathogens

Unmet needs

- Staph coverage: FQ-resistant and MRSA
- Slower resistance development vs other FQ

**\$2 B MRSA Market**

Unmet needs

- Better efficacy, safety and resistance profile vs standard Rx
- Need for effective new ORAL agents
- Broad-spectrum coverage for polymicrobial infections with MRSA

Market Drivers

- Increasing MRSA incidence
- Potent MRSA activity
- Favorable resistance profile
- IV & oral formulation

Estimated Peak Sales: ABSSSI (skin) and pneumonia, PYS ~ \$1.1 billion - ABSSSI indication only, PYS ~\$875 million Source: LEK