



SYNTHETIC

B I O L O G I C S

NYSE MKT: SYN

The Peggy Lillis Foundation
C. diff Advocates Summit

SYN-004: Microbiome Protection & C. difficile Prevention

Forward-Looking Statements

This presentation includes forward-looking statements on Synthetic Biologics' current expectations and projections about future events. In some cases forward-looking statements can be identified by terminology such as "may," "should," "potential," "continue," "expects," "anticipates," "intends," "plans," "believes," "estimates," "indicates," and similar expressions. These statements are based upon current beliefs, expectations and assumptions and are subject to a number of risks and uncertainties, many of which are difficult to predict and include statements regarding our clinical trials, our establishment of collaborations and our execution of our growth strategy. The forward-looking statements are subject to risks and uncertainties that could cause actual results to differ materially from those set forth or implied by any forward-looking statements. Important factors that could cause actual results to differ materially from those reflected in Synthetic Biologics' forward-looking statements include, among others, a failure of our product candidates to be demonstrably safe and effective, a failure to initiate clinical trials and if initiated, a failure to achieve the desired results, a failure to obtain regulatory approval for our product candidates or to comply with ongoing regulatory requirements, regulatory limitations relating to our ability to promote or commercialize our product candidates for the specific indications, a lack of acceptance of our product candidates in the marketplace, a failure of us to become or remain profitable, a failure to establish collaborations, our inability to obtain or maintain the capital or grants necessary to fund our research and development activities, a loss of any of our key scientists or management personnel, and other factors described in Synthetic Biologics' annual report on Form 10-K for the year ended December 31, 2014, subsequent quarterly reports on Form 10-Qs and any other filings we make with the SEC. The information in this presentation is provided only as of the date presented, and Synthetic Biologics undertakes no obligation to update any forward-looking statements contained in this presentation on account of new information, future events, or otherwise, except as required by law.

Collateral Damage Caused by Antibiotic Use

Imbalance of the gut microbiome

- Antibiotics
 - Prevent/treat primary infections
 - Carried to liver, transported to bile and excreted via large intestine
 - May unintentionally upset natural balance of gut microbiome by killing off good bacteria
- A microbial imbalance in the gut microbiome provides an opportunity for overgrowth of harmful pathogenic organisms (e.g., *C. difficile*) which may cause severe diarrhea, damage to the colon and in some cases death

**24 million patients are administered
IV antibiotics annually in the U.S.¹**

¹This information is an estimate derived from the use of information under license from the following IMS Health Incorporated information service: CDM Hospital database for full year 2012. IMS expressly reserves all rights, including rights of copying, distribution and republication.

LETTERS TO THE EDITORS

The Editors do not hold themselves responsible for opinions expressed by their correspondents. They cannot undertake to return, or to correspond with the writers of, rejected manuscripts intended for this or any other part of NATURE. No notice is taken of anonymous communications.

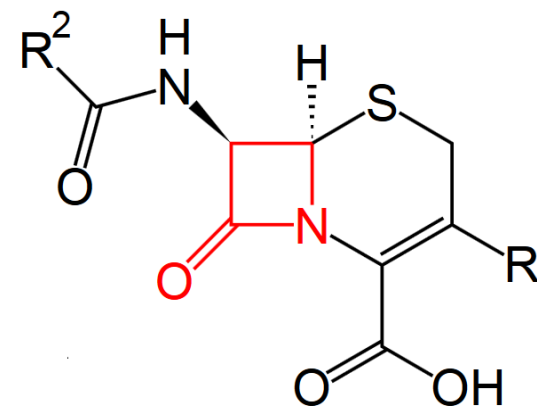
IN THE PRESENT CIRCUMSTANCES, PROOFS OF "LETTERS" WILL NOT BE SUBMITTED TO CORRESPONDENTS OUTSIDE GREAT BRITAIN.

An Enzyme from Bacteria able to Destroy Penicillin

FLEMING¹ noted that the growth of *B. coli* and a number of other bacteria belonging to the coli-

B. coli, it was not necessary to crush the organism in the bacterial mill in order to obtain the enzyme from it; the latter appeared in the culture fluid. The enzyme was also found in *M. lysodeikticus*, an organism sensitive to the action of penicillin, though

- Letter to Editor of Nature 1940: "An enzyme from bacteria able to destroy penicillin"
- First called penicillinases, later β -lactamases



In red: β -lactam ring common to penicillins and cephalosporins

SYN-004 – The deliberate preventive use of a β -lactamase to destroy unwanted antibiotics

- SYN-004 is **produced** in large quantities by bacteria that express the proprietary β -lactamase, purified and converted into drug product
- SYN-004 represents our **next generation** beta-lactamase enzyme
 - Developed from predecessor P1A – single amino acid change
- Expected to have **activity** against both penicillins and certain cephalosporins
- SYN-004 is an oral enzyme tablet to be co-administered with IV antibiotics
- IV antibiotics can upset the natural balance of the gut microbiome allowing for the **overgrowth of *C. difficile***
- SYN-004 is intended to remain in the GI tract and **neutralize IV antibiotics**, protecting the natural balance of the gut microbiome
- **Co-administration of SYN-004** is intended to allow the IV antibiotic to treat the primary infection while protecting the gut microbiome and preventing *C. difficile* infection

SYN-004 – How it works

To view the SYN-004 mechanism of action video, please visit: <http://www.syntheticbiologics.com/SYN-004>.



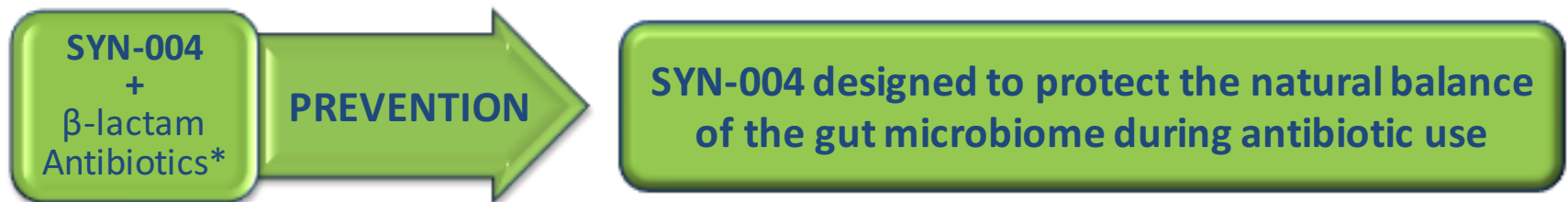
Paradigm Shift

Fewer CDIs expected with co-administration of SYN-004

Current Paradigm



SYN-004 Paradigm



* Intended to include penicillins plus cephalosporins

SYN-004

Clinical trial development

- Completed Phase 1a (40 participants) and 1b (24 participants) trials
 - PK data supports that SYN-004 should have no effect on the IV antibiotic in the bloodstream
 - No clinically significant safety events were observed; well tolerated by participants
- Initiated first Phase 2a trial (March 2015)
 - Characterize SYN-004 activity on ceftriaxone in the small intestine
 - Demonstrate SYN-004 has no activity on ceftriaxone in the bloodstream
 - SYN-004 degraded ceftriaxone in the chyme of initial four of 12 expected healthy participants with functioning ileostomies without affecting ceftriaxone in the bloodstream (July 2015)
- Initiated second Phase 2a trial (June 2015)
 - Characterize SYN-004 activity on ceftriaxone in the small intestine in the presence of esomeprazole, an approved, over-the-counter proton pump inhibitor
- **Phase 2b (Proof-of-Concept) trial objectives (initiation expected 3Q 2015)**
 - Plan to enroll ~370 patients in randomized, multi-center, placebo-controlled trial at ~75 global clinical sites
 - Demonstrate SYN-004 efficacy at preventing *C. difficile*-associated diarrhea (CDAD) and AAD following IV ceftriaxone
 - Demonstrate SYN-004 efficacy at limiting disruption of the gut microbiome by IV ceftriaxone
- FDA Type C meeting requested (trial design and endpoints)
- Phase 3 trial vision
 - Prevention of CDAD and AAD among hospitalized patients receiving IV ceftriaxone and other beta-lactam antibiotics
 - Global study; multiple indications for IV beta-lactam therapy
 - Demonstrate no effect on blood levels of antibiotic or primary diagnosis cure rates



SYNTHETIC

B I O L O G I C S

NYSE MKT: SYN

The Peggy Lillis Foundation

C. diff Advocates Summit

SYN-004: C. difficile Prevention

Klaus Gottlieb, MD, FACG, Vice President, Clinical & Regulatory Affairs
August 21, 2015

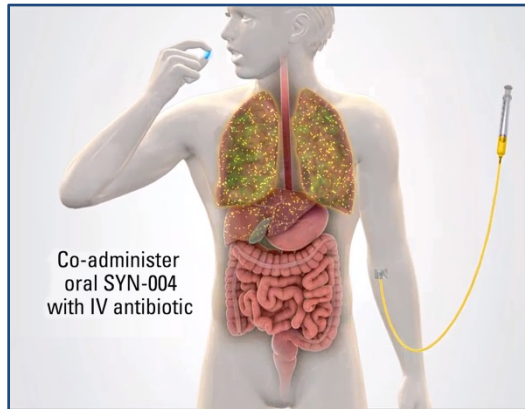


Backup

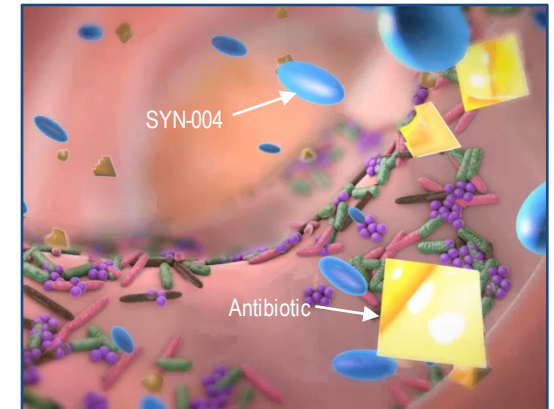
SYN-004 Co-Administered with IV Antibiotics

Designed to neutralize β -lactam antibiotics in GI tract

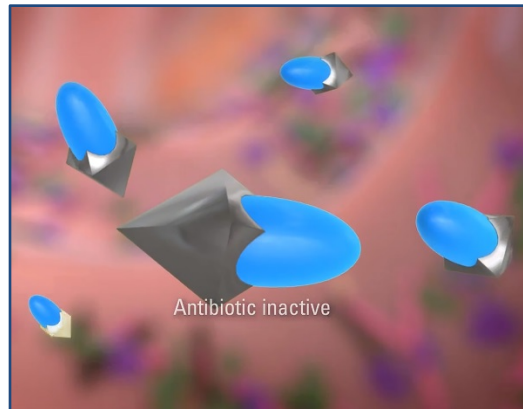
1. SYN-004 is an oral enzyme tablet (blue) to be co-administered with IV antibiotics (yellow).



2. IV antibiotics can upset the natural balance of the gut microbiome, killing “good” bacteria, allowing for the overgrowth of *C. difficile*.



3. SYN-004 is intended to remain in the GI tract and neutralize IV antibiotics (black), protecting the natural balance of the gut microbiome.



4. Co-administration of SYN-004 is intended to allow the IV antibiotic (yellow) to treat the primary infection while protecting the gut microbiome (blue), and preventing CDI.

