Lessons Learned in Developing SYN-004: a Potential Point-of-Care Preventative for HA-CDI

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Corporate and Product Development

Synthetic BIOLOGICS

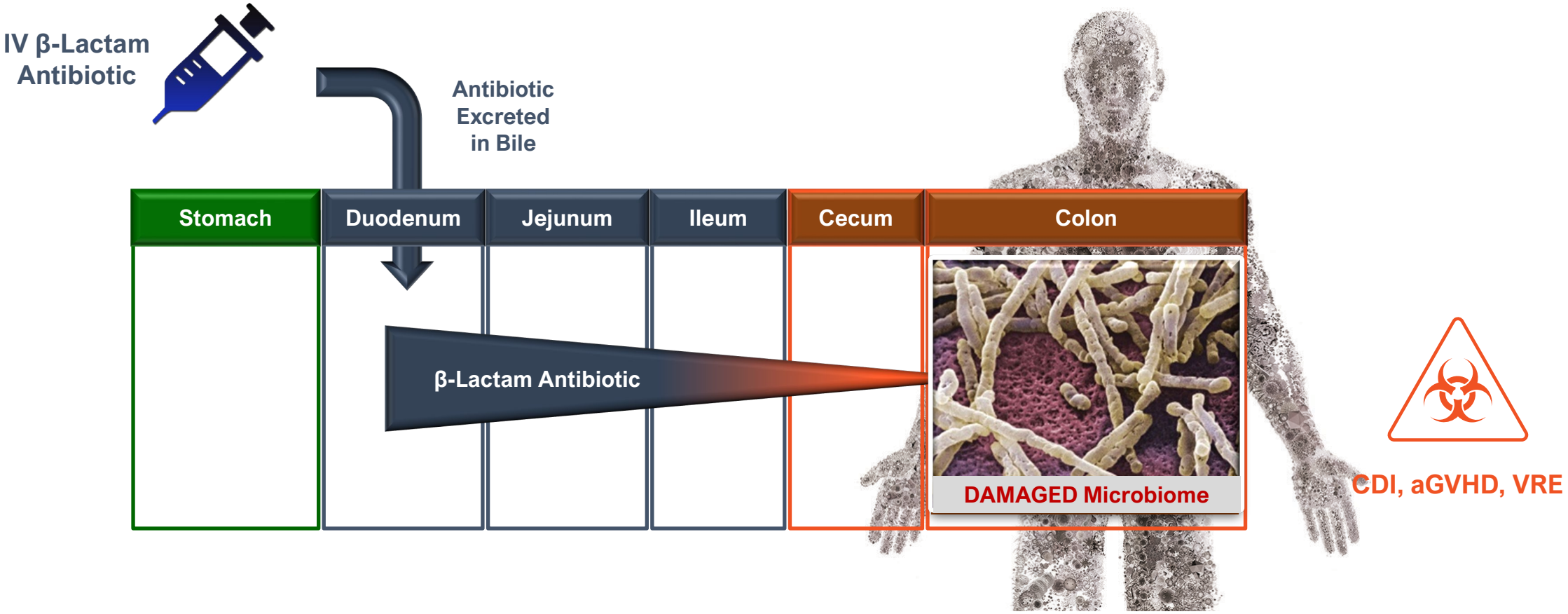
Prevention of Healthcare-Associated Infections

Forward-Looking Statements

This presentation includes forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. In some cases forward-looking statements can be identified by terminology such as "may," "should," "potential," "continue," "expects," "anticipates," "intends," "plans," "believes," "estimates," and similar expressions, and include statements regarding the potential of VCN-11 to balance safety, the suggestion that treatment with VCN-01 is feasible has an acceptable safety profile, the SAD and MAD studies supporting the development of SYN-020 in multiple clinical indications, initiation of VCN-01 dosing in an investigator sponsored study of brain tumors at the University of Leeds (H2 2022) initiation of VCN-01 dosing in combination with mesothelin-directed CAR-T cells for pancreatic and ovarian cancer in an investigator sponsored study at the University of Pennsylvania (H1 2022), initiation of a Phase 2 study of VCN-01 in combination with standard-of-care chemotherapy (gemcitabine/nab-paclitaxel) as a first line therapy in newly diagnosed metastatic PDAC patients (Q4 2022), initiation of a Phase 2/3 trial of VCN-01 as either an adjunct to chemotherapy or a potential rescue therapy in pediatric patients with advanced retinoblastoma (late 2023), data read out from the first cohort of the SYN-004 study in allo-HCT patients (H2 2022), being well positioned to deliver on our sharpened clinical development strategy and being poised for an exciting year ahead with the anticipation of multiple clinical studies and milestones that should continue to drive shareholder value and the potential for each of our clinical programs. These forward-looking statements are based on management's expectations and assumptions as of the date of this press release and are subject to a number of risks and uncertainties, many of which are difficult to predict that could cause actual results to differ materially from current expectations and assumptions from those set forth or implied by any forward-looking statements. Important factors that could cause actual results to differ materially from current expectations include, among others, whether the combined business of Synthetic Biologics and VCN will be successful, Synthetic Biologics' and VCN's product candidates demonstrating safety and effectiveness, as well as results that are consistent with prior results, the ability to initiate VCN-01 dosing in an investigator sponsored study of brain tumors at the University of Leeds (H2 2022), initiate VCN-01 dosing in combination with mesothelin-directed CAR-T cells for pancreatic and ovarian cancer in an investigator sponsored study at the University of Pennsylvania (H1 2022), initiate a Phase 2 study of VCN-01 in combination with standard-of-care chemotherapy (gemcitabine/nab-paclitaxel) as a first line therapy in newly diagnosed metastatic PDAC patients (Q4 2022), initiate a Phase 2/3 trial of VCN-01 as either an adjunct to chemotherapy or a potential rescue therapy in pediatric patients with advanced retinoblastoma (late 2023), data read out from the first cohort of the SYN-004 study in allo-HCT patients (H2 2022), the SAD and MAD studies supporting the development of SYN-020 in multiple clinical indications; the ability to complete clinical trials on time and achieve the desired results and benefits, continuing clinical trial enrollment as expected; the ability to obtain regulatory approval for commercialization of product candidates or to comply with ongoing regulatory requirements, regulatory limitations relating to Synthetic Biologics' and VCN's ability to promote or commercialize their product candidates for the specific indications, acceptance of product candidates in the marketplace and the successful development, marketing or sale of Synthetic Biologics' and VCN's products, developments by competitors that render such products obsolete or non-competitive, Synthetic Biologics' and VCN's ability to maintain license agreements, the continued maintenance and growth of Synthetic Biologics' and VCN's patent estate, the ability to continue to remain well financed, and other factors described in Synthetic Biologics' Annual Report on Form 10-K for the year ended December 31, 2021 and its other filings with the SEC, including subsequent periodic reports on Forms 10-Q and 8-K. The information in this release is provided only as of the date of this release, and Synthetic Biologics undertakes no obligation to update any forward-looking statements contained in this release on account of new information, future events, or otherwise, except as required by law.

SYN-004 (ribaxamase) to Prevent Microbiome Damage

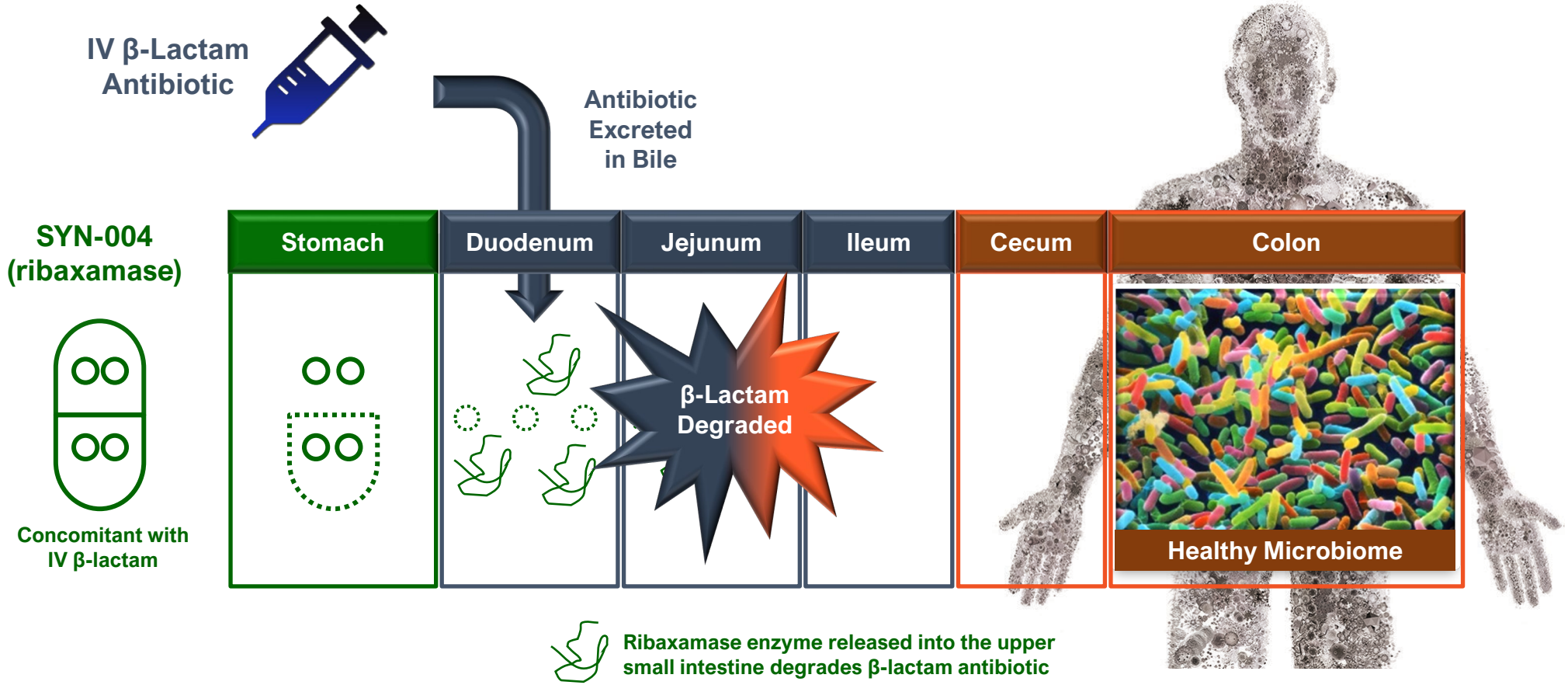
Antibiotic damage to the microbiome can cause disease



[1]Kokai-Kun JF et al. (2019) *Lancet Infect Dis* **19:**487-96. **CDI** *Clostridioides difficile* infection. **aGVHD** acute graft-vs-host disease. **VRE** vancomycin resistant enterococci.

SYN-004 (ribaxamase) to Prevent Microbiome Damage

Preserving the gut microbiome to prevent disease



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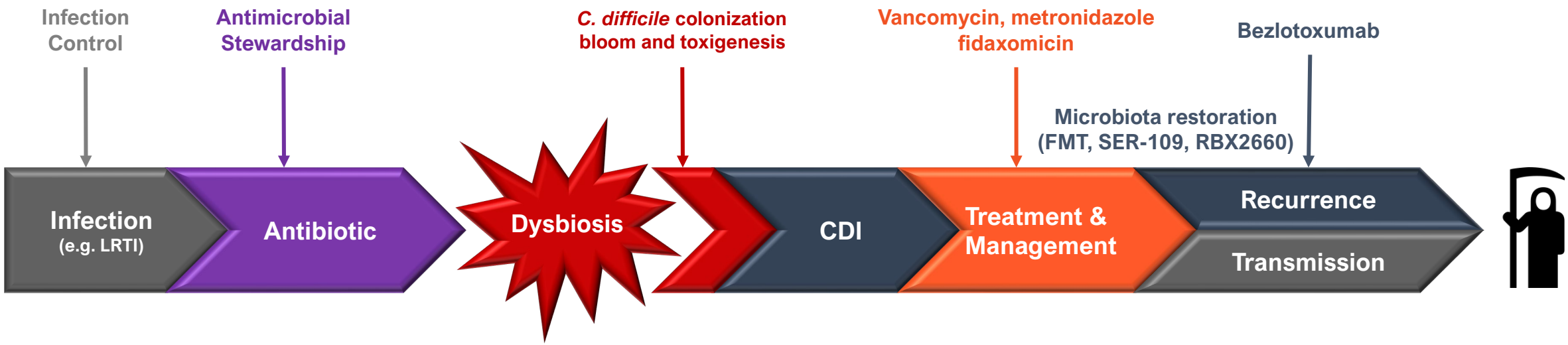
HA-CDI from Antibiotic Use

Simplified HA-CDI direct cost model



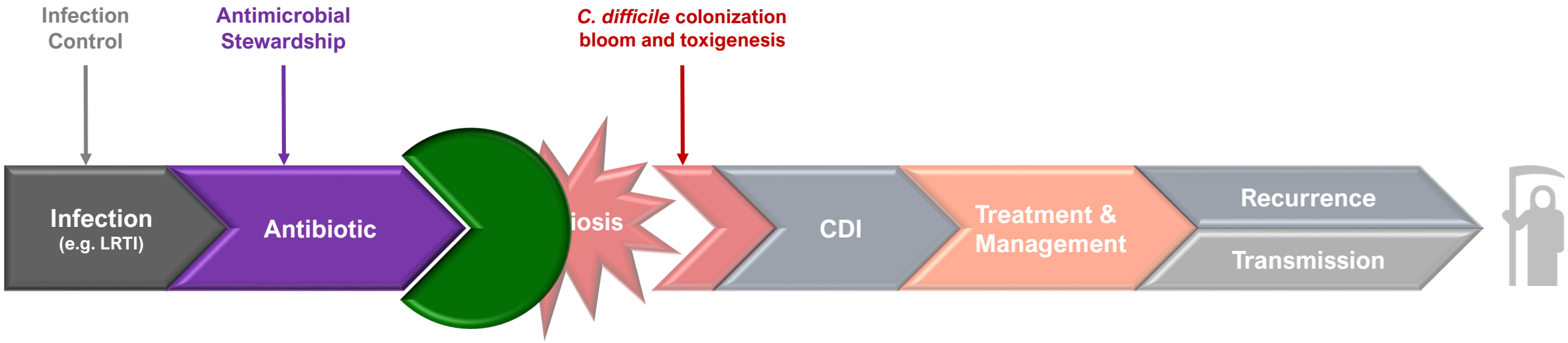
Patients (n)	**1,000**	**34 (3.4%)[1]**	**10**	**+$810,000***
Cost	**DRG**	**+$510,000[2]**	**+$300,000[3,4]**	

***Not** including
Mortality
Patient burden
HACRP Penalties
Liabilities

[1]Kokai-Kun (2019) *Lancet Infect Dis* **19:**487-96. [2]Current example uses $15,000 per patient for incident CDI and $30,000 per patient for recurrent CDI, Shah (2016) *J Hospital Infect* **93:**286-9, Zhang (2016) *BMC Infect Dis* **16:**447, Kwon (2015) *Infect Dis Clin N Am* **29:**123, Gabriel (2014) *J Hospital Infect* **88:**12. [3]CDI recurrence (20-40%) McFarland (2002) *Am J Gastroenterol* **97:**1769, Durovic (2017) *Infect Control Hosp Epidemiol* **38:**891. [4]Hospital transmission rate of CDI (1-2%) Durham (2016) *Emerg Infect Dis* **22:**608-16, Widmer (2017) *Clin Infect Dis* **64:**393-400. **DRG** diagnosis related group

Point-of Care Prevention of HA-CDI from Antibiotic Use

Simplified HA-CDI prevention cost-savings model



Patients (n)	**1,000**	**1,000**	**10 (1.0%)[1]**	**3**
Cost	**DRG**	***$???***	**+$150,000[2]**	**+$90,000[3,4]**

+$240,000*

Challenging to determine "hard" value

***Not** including
Mortality
Patient burden
HACRP Penalties
Liabilities

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Developing Drugs to Prevent HA-CDI - Lessons Learned

1. Trials are Large and Costly

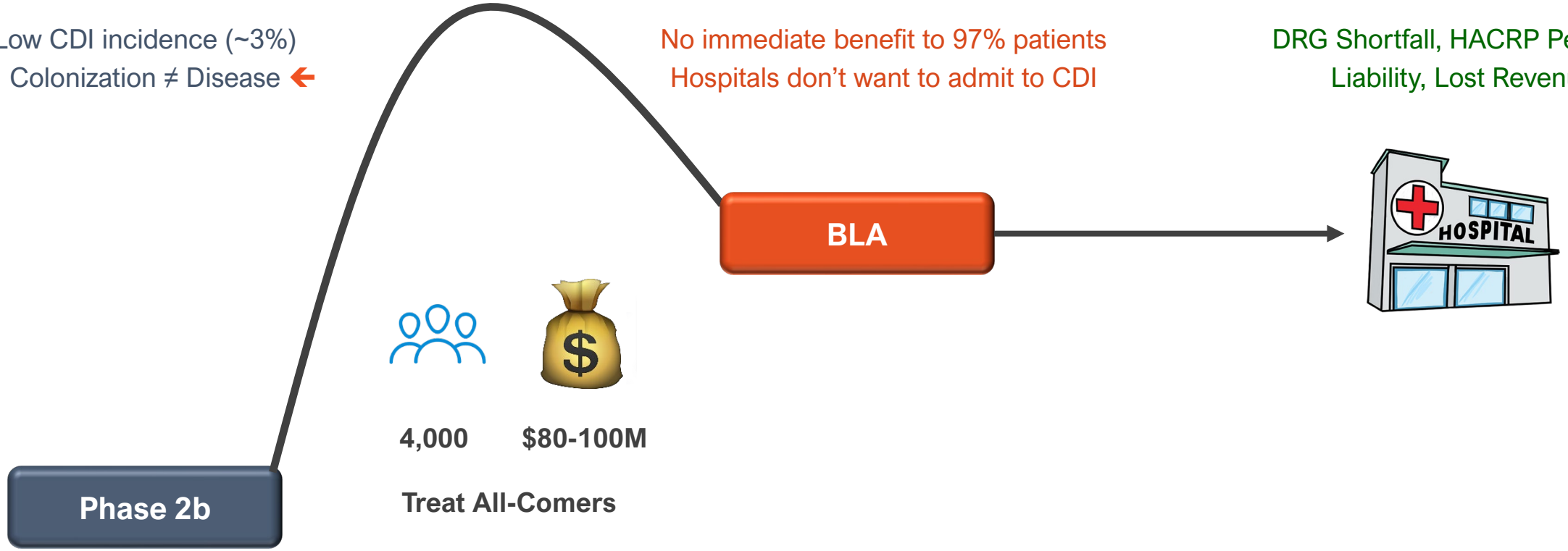
Low CDI incidence (~3%)
➔ Colonization ≠ Disease ➔

2. Trial Recruitment is Difficult

No immediate benefit to 97% patients
Hospitals don't want to admit to CDI

3. Hospitals are the 1° Customer

DRG Shortfall, HACRP Penalties
Liability, Lost Revenue



DRG diagnosis related group. **HACRP** Hospital Acquired Condition Reduction Program penalties are 1% of all hospital Medicare reimbursements for lowest performing 25% of hospitals. **Image Credit:** Hospital http://clipart-library.com/clipart/kTKBGA5zc.htm.

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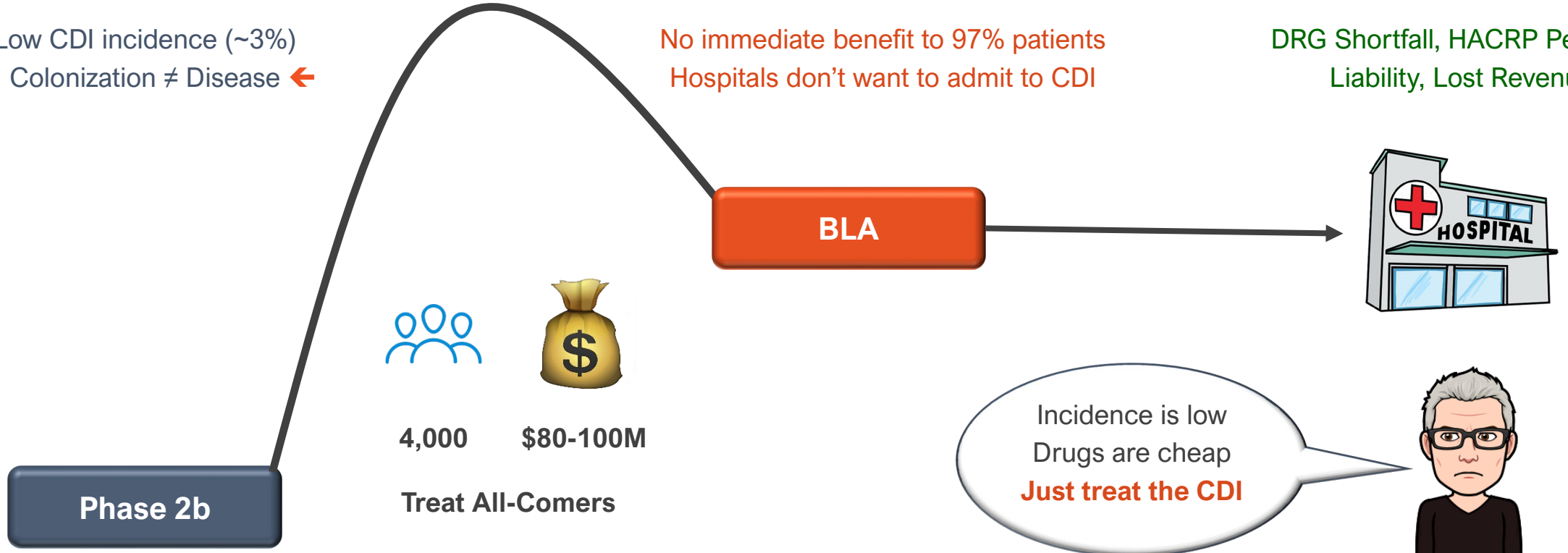

Actual feedback major pharma executive

4. Value Perception Problem

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How to Help HA-CDI Prophylactic Drug Development

- Identify CDI risk factors that enable patient preselection
- Agree on CDI biomarkers that can be used as approvable endpoints
- Conduct clinical trials in patient populations with a high incidence of CDI

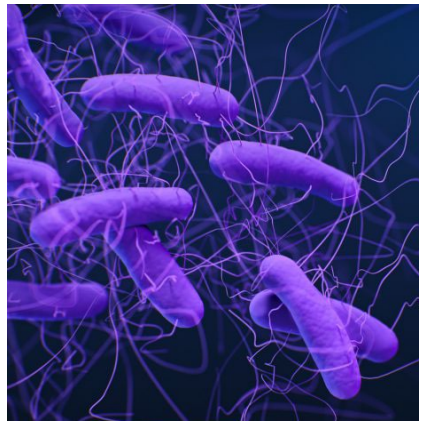

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Image Credit: *Clostridioides difficile* https://www.cdc.gov/drugresistance/solutions-initiative/stories/c-diff-diagnosis.html

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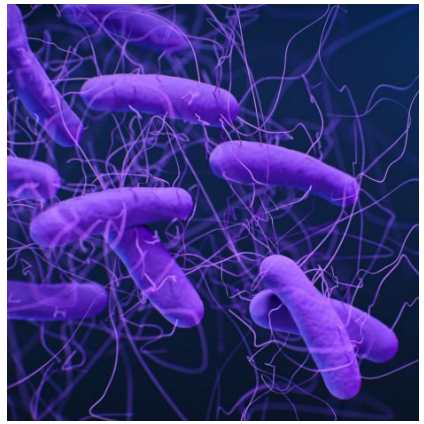
"But beyond just the money, it's also the morbidity and mortality that we were talking about before, right? And that, I think, from a clinician's standpoint, **our job is to heal people and to help them** make it so that—so you can take care of things in the right way."

Chief Medical Officer - 396 Bed Community Hospital



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