How Novavax is Innovating a New Vaccine Approach to Address C. Diff and Expand into Bacterial Diseases

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Since we refocused Novavax in 2025 to maximize the impact of our technology through **R&D innovation** **and strategic partnerships**, we have searched for opportunities that address a significant unmet need for patients while also providing a differentiated commercial opportunity to ensure we're bringing value to our stakeholders. This search led us directly to Clostridioides difficile (C. difficile or C. diff). This type of bacteria leads to C. difficile infection (CDI) which causes toxin-mediated colitis, or colon inflammation, that is often associated with significant morbidity and mortality.

Why is C. diff such a persistent problem? It forms spores that are **nearly indestructible and can persist in the gut of infected patients and on surfaces for months**. This is a big deal in hospitals — regular cleaning often isn't enough, and bleach-based products are required to kill the spores. This can mean it **spreads easily in healthcare settings**. Once CDI takes hold, it **produces toxins** that damage the lining of the colon, causing inflammation, abdominal pain, severe watery diarrhea and, in bad cases, a life-threatening condition called pseudomembranous colitis or toxic megacolon.

Despite the impact of these bacteria, options to prevent infections are limited. There are currently **no U.S. Food and Drug Administration–approved vaccines** for the prevention of CDI. Antibiotics are the main approach but can also backfire because C. diff actually **thrives when antibiotics wipe out the normal gut flora** (which act as competition). The gut normally hosts a huge, diverse community of bacteria that keeps C. diff in check. Broad-spectrum antibiotics — even ones given for a totally unrelated infection — can kill off that protective microbiome, leaving an empty niche that C. diff spores exploit to bloom out of control. In fact, **over 30% of patients get it again**.[1]

From a patient perspective, the need is clear. From a company perspective, C. diff represents a **significant unmet market opportunity** with approximately 500,000 cases of C. diff occurring each year in the U.S.[2] In addition, more than 20,000 in-hospital deaths from C. diff occur annually in the U.S.[3] C. diff represents an opportunity for Novavax to potentially offer a best-in-class treatment, in addition to allowing the Company to expand from a focus on viral disease to bacterial disease as well.

At Novavax, we've had the opportunity to learn from the prior vaccine development efforts of others. This has led to the creation of our vaccine candidates that are anchored on our proven Matrix-M® adjuvant technology. Our C. diff candidates use a multivalent antigen approach containing toxin and non-toxin components that target a vast majority of circulating clades and ribotypes. Our approach also focuses beyond toxin neutralization – a potential limitation of previous vaccine candidates – to also address mucosal immunity, killing the bacteria and preventing or reducing the severity of C. diff-associated disease.

We have recently generated encouraging preclinical data for our vaccine candidates. At the 9th International C. Difficile Symposium today, we presented data that showed our C. diff vaccine candidates generated **robust immune responses and protection** in two lethal challenge models. Three vaccine constructs – Q-Tox, P-Tox and C-Tox – were evaluated, with **P-Tox emerging as the current lead candidate**. The P-Tox candidate **demonstrated greater survival** than the toxoid comparator following lethal C. diff spore and toxin B challenges in preclinical models.

Following challenge with spores from the hypervirulent C. diff NAP1 strain, 75% (n=6/8) of hamsters immunized with P-Tox survived, compared with only 25% (n=2/8) of those receiving a toxoid comparator. In a separate toxin B challenge model, 100% (n=10/10) of mice receiving P-Tox at the evaluated 3-?g dose survived compared with 80% (n=8/10) of those receiving the toxoid comparator at the evaluated 10-?g dose. P-Tox vaccination also reduced the severity of C. diff–associated intestinal damage following spore challenge.

Our preclinical work shows **the potential of our vaccine technology** to generate broad immune responses and protect against C. diff-mediated disease. We remain on track to advance the program into clinical development as early as 2027.

References

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