Figure 1. Return on Investment Sensitivity Analysis for Fexinidazole (Source: Authors' calculations)

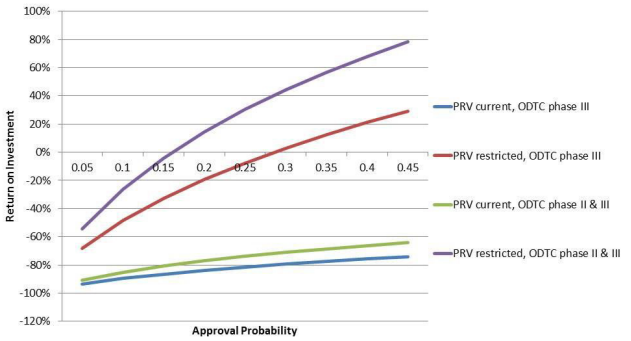
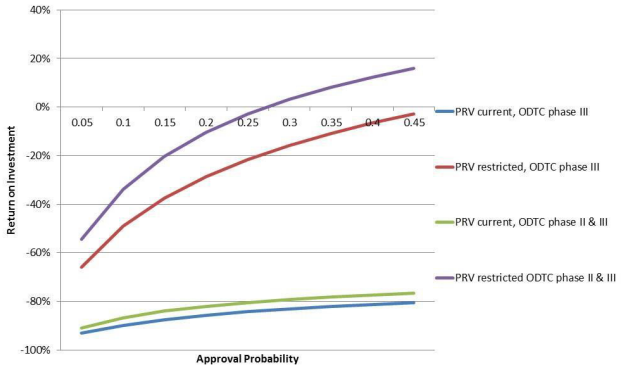


Figure 2. Return on Investment Sensitivity Analysis for Acoziborole (Source: Authors' calculations)



Conclusion. We find support for NTD drug development within the private sector, but no novel R&D without nonprofit stewardship. Our findings intend to foster PPPs that stimulate this pipeline from very low current levels.

Disclosures. **All Authors**: No reported disclosures

1235. On the Edge of Tomorrow: Expedited Regulatory Pathways for Anti-Infective Therapies

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Session: P-56. New Drug Development

Background. The FDA has developed expedited review programs and pathways to increase drug development for products that have a major clinical benefit. These programs include: Fast Track, Orphan Drug Status, Accelerated Approval, Priority Review, Breakthrough Therapy (BTD) and Qualified Infectious Disease Products (QIPD).

Given the heightened awareness of infectious diseases--and emerging global threats, such as resistant bacteria and Ebola—academia and industry have developed and received approval for 88 new infectious disease agents. The objective of this study was to assess the use of expedited review pathways for the 88 anti-infective agents that were approved between 2001-2020.

FDA Expedited Drug Development Programs

FDA Expedited Drug Development Programs

Program Type	Explanation
Fast Track Designation	Fast track designation is available for drugs that are intended to treat serious conditions and show data addressing an unmet need.
Priority Review	Priority review ensures a new drug application will be reviewed within a 6 month window instead of the conventional 10 months.
Accelerated Approval	Accelerated approval is considered when a drug provides a meaningful advantage over current therapies through a surrogate endpoint that is likely correlated to a clinical benefit; the "conditional" approval is contingent upon verification of the benefit in future confirmatory trials.
Orphan Drug Status	Orphan drug status is available for drugs intended to treat rare diseases where the sponsor receives various incentives including tax credits for clinical trials.
Qualified Infectious Disease Product	Through the GAIN Act that was passed in 2012, drugs in development may be designated as a qualified infectious disease product (QIDP) if they are targeting certain types of infectious diseases. QIDPs are eligible for fast track and priority review status.
Breakthrough Therapy	Breakthrough therapy designation is typically received early in drug development when the IND (investigational new drug) is filed, where the sponsor receives significant guidance on their drug development program from the FDA.

Methods: We analyzed the FDA Drug Approval Database entitled, "Compilation of CDER New Molecular Entity (NME) Drug and New Biologic Approvals" for anti-infective therapies that were approved after 2000. Anti-infective therapies were defined as agents that were used to treat or prevent infectious diseases and include antibiotics, antivirals and antifungals. Our analysis focused on a comparison of the percentage of approved anti-infective agents that used each of the aforementioned designations across 2 decades (2001-2010 & 2011-2020). A drug may have one, none, or multiple of these designations.

Results. There were significant differences in the percentage of anti-infective agents approved with priority review, fast track and accelerated approval in 2001-2010 compared to 2011-2020 (See Results Figure 1) BTD and QIDP did not exist until 2012, thus preventing comparisons between decades.

QIDP.
- Between 2012-2020, 16 anti-infectives have been approved with QIDP. From 2017-2020, 40% (n=10) of approved anti-infectives had QIDP.

Orphan Drug Status:
- Between 2017-2020, 32% of anti-infectives approved have the orphan drug designation.

Comparison of FDA Expedited Drug Development Programs use between 2001-2010 and 2011-2020

Comparison of FDA Expedited Drug Development Programs use between 2001-2010 and 2011-2020

Program Type	% of Products Approved via Program Type in 2001-2010	% of Products Approved via Program Type in 2011-2020	P Value
Fast Track Designation*	49%	78%	0.007
Priority Review *	31%	60%	0.004
Accelerated Approval *	18%	3%	0.03
Orphan Drug Status	5%	19%	0.07
Qualified Infectious Disease Product^	N/A	35%	N/A
Breakthrough Therapy^	N/A	17%	N/A

*P Value less than .05
^Programs started in 2012

Conclusion. Our findings indicate Priority Review and Fast Track use has increased since 2010 among anti-infective products. Additionally, our analyses indicate that since 2017 there has been increased use of Orphan Drug Status and QIDP. However, there has been limited use of Breakthrough Therapy and Accelerated Approvals. These two pathways should be increasingly considered by academia, industry and the FDA to further expedite innovative anti-infective development.

Disclosures. **All Authors**: No reported disclosures

1236. Safety and Immunogenicity of a 20-Valent Pneumococcal Conjugate Vaccine (PCV20) in Healthy Infants in the United States

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Session: P-56. New Drug Development

Background. A 20-valent pneumococcal conjugate vaccine (PCV20) is being developed to extend protection against pneumococcal disease beyond that of the 13-valent pneumococcal vaccine (PCV13). This is the first safety and immunogenicity study of PCV20 in healthy infants.

Methods. This randomized, double-blind study enrolled and randomized (1:1) healthy infants ≥ 42 to ≤ 98 days of age to receive a 4-dose series of either PCV20 or PCV13 (control) at 2, 4, 6, and 12 months of age. Local reactions and systemic events were assessed for 7 days after each vaccination; adverse events (AEs) and serious AEs (SAEs) were collected throughout the study. PCV20 immune responses (serotype-specific immunoglobulin G [IgG] and opsonophagocytic activity [OPA]) were measured in sera 1 month after the third infant dose and the fourth dose at 12 months of age.

Results. There were 460 subjects enrolled, with 416 and 391 subjects receiving 3 and 4 doses, respectively. Local reactions and systemic events were predominantly mild to moderate in severity and similar among vaccine groups. There were no related SAEs or deaths reported. PCV20 elicited IgG responses 1 month after the third dose with boosting after a fourth dose. OPA responses were also observed.

Conclusion. PCV20 was well tolerated with a safety profile similar to PCV13. PCV20 elicited immune responses to all 20 vaccine serotypes.

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1237. Robust Adjuvant Activity and Dose-sparing Potential of the Novel Semisynthetic Saponin Adjuvant TQL1055 for Seasonal and Pandemic Influenza

Chloe Buzz, BS[1]; Eric Farris, PhD[1]; Sean R. Bennett, MD PhD[2]; Pat Frenchick, PhD[1]; Tyler Martin, MD[1]; [1]Adjuvance Technologies, Lincoln, Nebraska; [2]Adjuvance Technologies, Inc., Lincoln, Nebraska

Session: P-57. New Vaccines

Background. Vaccination against both seasonal and pandemic influenza requires effective adjuvants to maximize the utility of limited antigen and to enhance immunogenicity in hyporesponsive at-risk populations. First-generation natural saponins are potent immuno-enhancers but are reactogenic and have supply constraints. As part of

a NIH-funded project, the novel semisynthetic saponin TQL1055 was evaluated for its potential to augment the immunogenicity of influenza antigens.

Figure 1: TQL1055 Enhances the Antibody Response to a Recombinant Antigen Influenza Vaccine (Flublok®) and Exhibits Antigen Dose-Sparing Effects

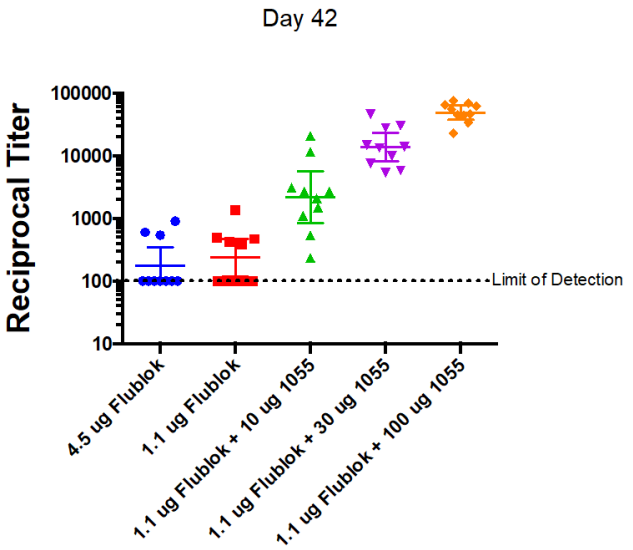
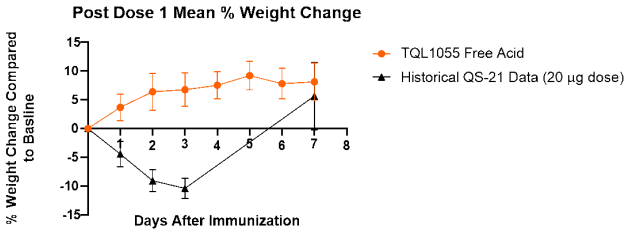


Figure 2: TQL1055 Exhibits Improved Systemic Tolerability Over QS-21.



Methods: Groups of 10 C57BL/6J mice were immunized subcutaneously (SC) with Flublok® (H3N2 antigen) alone at either a 4.5 mcg or 1.1 mcg dose, or at a 1.1 mcg dose in combination with 10, 30 or 100 mcg TQL1055 on Days 0 and 21. Sera were analyzed at days 0, 21 and 42 by ELISA for H3N2-specific IgG. Body weights were measured serially.

Results. A 2-dose series of 1.1 mcg Flublok with TQL1055 elicited anti-H3N2 antibodies in all mice. This effect was TQL1055 dose-dependent, with GMTs of 2178 in the 10 mcg group, 13674 in the 30 mcg group and 48959 in the 100 mcg group. The GMT in all TQL1055 groups was higher than the GMT of 176 in the group receiving 4.5 mcg of Flublok alone. Mice receiving TQL1055 gained weight steadily after immunization, compared with a maximum weight loss of >10% in mice receiving 20 mcg of QS-21.

Conclusion. TQL1055 exhibits robust adjuvant activity for influenza antigens, demonstrating a dose-sparing effect and improved systemic tolerability compared with QS-21. Taken together, these finding support further evaluation of its potential as an adjuvant for influenza vaccines.

Disclosures. Chloe Buzz, BS, Adjuvance Technologies (Employee) Eric Farris, PhD, Adjuvance Technologies (Employee) Sean R. Bennett, MD PhD, Adjuvance Technologies (Employee) Pat Frenchick, PhD, Adjuvance Technologies (Consultant) Tyler Martin, MD, Adjuvance Technologies (Employee, Shareholder)

1238. The Novel Semisynthetic Saponin Adjuvant TQL1055 Enhances the Antibody Response to Pertussis Vaccine with an Improved Tolerability Profile over QS-21

Chloe Buzz, BS[1]; Govind Ragupathi, PhD[2]; Sean R. Bennett, MD PhD[3]; Phil Livingston, MD[1]; Eric Farris, PhD[1]; Tyler Martin, MD[1]; [1]Adjuvance Technologies, Lincoln, Nebraska; [2]Memorial Sloan Kettering Cancer Center, New York, New York; [3]Adjuvance Technologies, Inc., Lincoln, Nebraska

Session: P-57. New Vaccines

Background. Acellular pertussis vaccines are better tolerated but less immunogenic than older whole cell vaccines. Novel adjuvants may be useful to enhance their immunogenicity. First-generation natural saponins are potent immuno-enhancers but are highly reactogenic. The novel semisynthetic saponin TQL1055 was evaluated for its potential to enhance the immunogenicity of a commercially available acellular pertussis vaccine as part of a National Institute of Allergy and Infectious Disease (NIAID) funded project.

Methods. Groups of 10 female C57BL/6J mice were immunized subcutaneously (SC) with Adacel® (containing 0.5 mcg pertussis toxin antigen) alone or in combination with QS-21 at 20 mcg/dose or TQL1055 at 50 mcg/dose on Days 0 and 28. Serum antibody titer to pertussis antigen was determined by ELISA (Alpha Diagnostics) at Days 0, 28, and 42 and geometric mean titers (GMT) in IU/mL were determined. Body weights were measured serially for 7 days after dose 1.

Results. At 28 days following dose 1, mice receiving TQL1055 had an anti-pertussis toxin IgG GMT of 8492, compared with 2263 in mice receiving QS-21 ($p = 0.005$). At Day 42, 14 days after dose 2, the GMTs increased to 18719 in the TQL1055 group and 10851 in the QS-21 group ($p = 0.0653$ vs TQL1055 dose 2; $p = 0.6038$ vs TQL1055 dose 1). Mice in the Adacel and TQL1055 groups gained weight steadily after dose 1, while mice in the QS-21 group had an average weight loss of 10% from baseline at 3 days after dose 1 ($p < 0.0001$).

Figure 1: TQL1055 Enhances the Antibody Response to Adacel® (Commercial Acellular Pertussis Vaccine) in C57BL/6J Female Mice

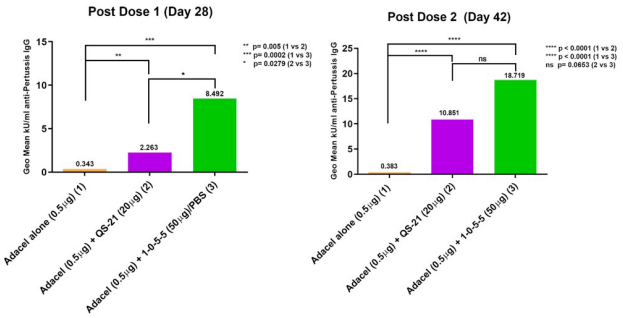
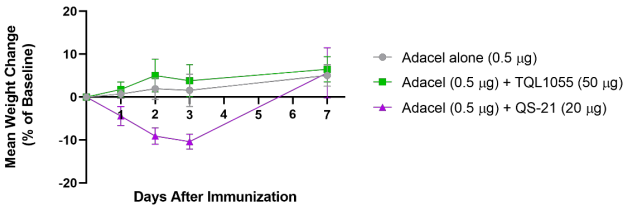


Figure 2: TQL1055 Shows Enhanced Tolerability (measured by decreased weight loss) Compared to QS-21 Following Subcutaneous Injection in C57BL/6J Female Mice



Conclusion: TQL1055 enhanced the antibody response to a commercial acellular pertussis vaccine to a greater degree than QS-21. Additionally, TQL1055 was better tolerated than QS-21, with no weight loss after vaccination. These findings suggested that TQL1055 may improve the performance of acellular pertussis vaccines without an increase in reactogenicity.

Disclosures. Chloe Buzz, BS, Adjuvance Technologies (Employee) Sean R. Bennett, MD PhD, Adjuvance Technologies (Employee) Phil Livingston, MD, Adjuvance Technologies (Consultant, Shareholder) Eric Farris, PhD, Adjuvance Technologies (Employee) Tyler Martin, MD, Adjuvance Technologies (Employee, Shareholder)

1239. Different Dose Levels of a Respiratory Syncytial Virus Maternal Vaccine Candidate (RSVPreF3) Administered to Non-pregnant Women in a Randomized Clinical Trial Are Immunogenic and Well Tolerated

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Session: P-57. New Vaccines

Background. Respiratory syncytial virus (RSV) is a leading cause of bronchiolitis and pneumonia in childhood. Maternal immunization could help to protect infants from RSV-associated infections in their first months of life. We evaluated the safety, reactogenicity and immunogenicity of the RSV maternal (RSVPreF3) vaccine candidate in non-pregnant women, at different dose levels.

Methods. In this phase I/II, observer-blind, multicenter study (NCT03674177), healthy non-pregnant women aged 18–45 years were randomized (1:1:1:1) and received 1 dose of either 30, 60 or 120 µg of RSVPreF3 vaccine (30/60/120 RSVPreF3 group) or placebo. Solicited adverse events (AEs) (until day 7 [D7] post-vaccination), unsolicited AEs (until D30 post-vaccination), hematological and biochemical laboratory abnormalities (at D8 and D31 post-vaccination) were recorded. Serious AEs (SAEs) were collected until D181 and immune responses until D91 post-vaccination. Exploratory analysis was performed at D31 to compare immunogenicity of different dose levels.