

Alison E. Heald, MD, MHS
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PROFESSIONAL SUMMARY

Over 15 years of clinical drug development experience with HIV vaccines, post-exposure prophylaxis of Ebola and Marburg viruses, rheumatoid arthritis, cystic fibrosis, ovarian cancer, and head and neck cancer. Expertise includes gene transfer, RNA targeting, and the Animal Rule.

EXPERIENCE

Alison Heald Consulting, LLC, Seattle, WA

2016 – present

Principal, Clinical Drug Development Services

- ♦ Clinical strategy
- ♦ Clinical trial design and implementation
- ♦ Clinical trial operations
- ♦ Medical monitoring
- ♦ Data safety monitoring board services
- ♦ Safety assessment committee services
- ♦ Clinical endpoint development
- ♦ Preparation of clinical documents for regulatory filings (IND, NDA, NIH-RAC)
- ♦ Interpretation and synthesis of clinical trial results
- ♦ Authoring of manuscripts, clinical study reports, and grant applications

University of Washington Medical Center, Seattle, WA

2000 – present

Attending Physician, Madison HIV Clinic

2000 – present

Clinical Associate Professor, Allergy and Infectious Diseases

2015 – present

Clinical Assistant Professor, Allergy and Infectious Diseases

2012 – 2015

Clinical Associate, Allergy and Infectious Diseases

2000 – 2012

Sarepta Therapeutics, Inc., Bothell, WA (formerly AVI BioPharma, Inc.)

2010 – 2014

Senior Director, Clinical Development

2010 – 2014

- ♦ Oversaw scientific and technical aspects of a contract with the Department of Defense to develop two modified phosphorodiamidate morpholino oligomer (PMO_{plus}) compounds, AVI-7288 and AVI-7537, as post-exposure prophylaxis for **Marburg virus** and **Ebola virus**, respectively.
 - Led strategy team meetings on product development of AVI-7288 and AVI-7537 in pursuit of FDA approval under the Animal Rule.
 - Designed, implemented, completed and published clinical studies to evaluate safety of the compounds in humans.
 - Provided medical monitoring services for phase 1 first-in-human clinical studies.
 - Effectively interacted with the FDA, amending the IND and participating in regulatory meetings.
- ♦ Provided guidance on the clinical development of AVI-7100, a PMO_{plus} compound with activity against influenza.

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Alder BioPharmaceuticals, Bothell, WA

2009 – 2010

Senior Medical Director

2009 – 2010

- ◆ Explored new oncology indications for an anti-IL-6 monoclonal antibody, including ovarian cancer, non-small cell lung cancer and multiple myeloma.
- ◆ Finalized clinical study reports for phase 1 and phase 2 clinical trials of an anti-IL-6 monoclonal antibody in healthy subjects, rheumatoid arthritis and non-small cell lung cancer.

Targeted Genetics Corporation, Seattle, WA

2000 – 2009

Senior Director, Clinical Affairs

2005 – 2009

Director, Clinical Affairs

2002 – 2005

Program Physician, Clinical Affairs

2000 - 2002

- ◆ Provided safety oversight of phase 1 and phase 2 **HIV vaccine** studies conducted by the International AIDS Vaccine Initiative (IAVI) in Europe, India and Africa, organizing and leading the Data Safety Monitoring Board.
- ◆ Wrote pertinent sections of the pre-IND and IND submissions for **HIV vaccine** study to be conducted in collaboration with the HIV Vaccine Trials Network (HVTN).
- ◆ Successfully guided a gene transfer product candidate for **rheumatoid arthritis** into phase 1 and phase 2 clinical trials.
 - Devised clinical development plan in consultation with thought leaders and experts.
 - Designed, implemented, completed and published phase 1 and 2 clinical trials.
 - Wrote pertinent sections of the IND application, negotiated details of the clinical trials with the FDA, and successfully interacted with the FDA about a highly-publicized fatal serious adverse event, leading to the release of clinical hold.
 - Assisted with preparation for public review of clinical trials by the NIH Recombinant DNA Advisory Committee (RAC).
 - Collaborated with Outcome Measures in Rheumatology Clinical Trials (OMERACT) to develop new outcomes to measure response of single joints to local therapy.
- ◆ Successfully designed, enrolled and completed a phase 2 clinical study of gene transfer product candidate for **cystic fibrosis**.
- ◆ Supervised conduct of the clinical trials and provided safety monitoring for phase 1 and phase 2 studies of **ovarian cancer** and **head and neck cancer**.

Duke University Medical Center, Durham, NC

1996 – 2000

Assistant Professor of Medicine, Infectious Diseases Division

1997 – 2000

Associate in Medicine, Infectious Diseases Division

1996 – 1997

- ◆ Served as principal investigator on corporate-sponsored HIV drug studies, AIDS Clinical Trials Group studies and National Institute of Drug Abuse grant.

University Hospital of Geneva, Geneva, Switzerland

1990 – 1992

Clinical Research Associate, Centre SIDA (AIDS Unit)

1990-1992

Research Associate, Policlinique de Médecine

1990

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SPECIALTY CERTIFICATION

American Board of Internal Medicine, Infectious Diseases
American Board of Internal Medicine, Internal Medicine

PHYSICIAN LICENSURE

License to Practice Medicine, Washington State

PROFESSIONAL TRAINING

Duke University Medical Center, Durham, NC
Fellowship in Infectious Diseases

Yale-New Haven Hospital, New Haven, CT
Residency in Internal Medicine

EDUCATION

University of Pennsylvania School of Medicine, Philadelphia, PA
Doctor of Medicine

- ◆ Honors: Alpha Omega Alpha

Duke University, Durham, NC
Masters of Health Sciences, Division of Biometry

Swarthmore College, Swarthmore, PA
Bachelor of Arts with Distinction

- ◆ Major field of study: Chemistry
- ◆ Honors: Phi Beta Kappa, Sigma Xi

PUBLICATIONS

1. **Heald A**, Ransohoff D. Needlestick injuries among resident physicians. *Journal of General Internal Medicine* 1990; 5:389-393.
2. Hirschel B, Lazzarin A, Chopard P, Opravil M, Furrer H-J, Rüttimann, S, Vernazza P, Chave J-P, Ancarani F, Gabriel V, **Heald A**, King R, Malinverni R, Martin J-L, Mermillod B, Nicod L, Simoni L, Vivirito MC, Zerboni R and the Swiss Group for Clinical Studies on AIDS. A controlled study of inhaled pentamidine for primary prevention of *Pneumocystis carinii* pneumonia. *New England Journal of Medicine* 1991; 324:1079-1083.
3. **Heald A**, Flepp M, Chave J-P, Malinverni R, Rüttimann S, Gabriel V, Renold C, Sugar A, Hirschel B and the Swiss HIV Cohort Study. Treatment for cerebral toxoplasmosis protects against *Pneumocystis carinii* pneumonia in patients with AIDS. *Annals of Internal Medicine* 1991; 115:760-763.
4. **Heald A**, Auckenthaler R, Borst F, Delaspre O, Germann D, Matter L, Kaiser L, Stalder H. Adult bacterial nasopharyngitis: a clinical entity? *Journal of General Internal Medicine* 1993; 8:667-73.
5. **Heald AE**, Bartlett JA. Cryptosporidium spread in a group residential home. *Annals of Internal Medicine* 1994; 121: 467-8.

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6. Opravil M, Pechère M, Lazzarin A, **Heald A**, Rüttimann S, Iten A, Furrer H-J, Oertle D, Praz G, Vuitton DA, Hirschel B, Lüthy R. Dapsone-pyrimethamine may prevent mycobacterial disease in immunosuppressed patients infected with the human immunodeficiency virus. *Clinical Infectious Diseases* 1995; 20:244-9.
7. Opravil M, Hirschel B, Lazzarin A, **Heald A**, Pechère M, Rüttimann S, Iten A, von Overbeck J, Oertle D, Praz G, Vuitton DA, Mainini F, Lüthy R. Once weekly dapsone-pyrimethamine versus aerosolized pentamidine as combined prophylaxis of *Pneumocystis carinii* pneumonia and toxoplasmic encephalitis in human immunodeficiency virus-infected patients. *Clinical Infectious Diseases* 1995; 20:531-41.
8. Graham CS, Graham BG, Bartlett JA, **Heald AE**, Schiffman SS. Taste and smell losses in HIV-infected patients. *Physiology and Behavior* 1995; 58:287-93.
9. **Heald AE**, Cox GM, Schell WA, Bartlett JA, Perfect JR. Oropharyngeal yeast flora and fluconazole resistance in human immunodeficiency virus (HIV) infected patients receiving long-term continuous vs. intermittent fluconazole therapy. *AIDS* 1996; 10:263-8.
10. **Heald AE**, Hsyu PY, Yuen GJ, Robinson P, Mydlow P, Bartlett JA. Pharmacokinetics of lamivudine in HIV-infected patients with renal dysfunction. *Antimicrobial Agents and Chemotherapeutics* 1996; 40:1514-9.
11. Kaiser L, Lew D, Hirschel B, Auckenthaler R, Morabia A, **Heald A**, Benedict P, Terrier F, Wunderli W, Matter L, Germann D, Voegeli J, Stalder H. Effects of antibiotic treatment in the subset of common-cold patients who have bacteria in nasopharyngeal secretions. *Lancet* 1996; 347:1507-10.
12. **Heald AE**, Hoffman JM, Bartlett JA, Waskin HA. Differentiation of central nervous system lesions in AIDS patients using positron emission tomography (PET). *International Journal of STD and AIDS* 1996; 7:337-46.
13. **Heald AE**, Schiffman SS. Taste and smell: neglected senses that contribute to malnutrition in AIDS. *North Carolina Medical Journal* 1997; 58:100-4.
14. **Heald AE**. Brain biopsy for HIV-infected patients with intracranial lesions. *North Carolina Medical Journal* 1997; 58:106-9.
15. **Heald AE**, Hicks CB. Clinical complications of HIV infection. *Radiologic Clinics of North America* 1997; 35:1007-27.
16. **Heald AE**, Pieper CF, Schiffman SS. Taste and smell complaints in HIV-infected patients. *AIDS* 1998; 12:1667-74.
17. Gottfredsson M, Cox GM, Indridason OS, de Almeida GMD, **Heald AE**, Perfect JR. Association of plasma levels of Human immunodeficiency virus type 1 RNA and oropharyngeal *Candida* colonization. *Journal of Infectious Diseases* 1999; 180:534-7.
18. Schiffman SS, Zervakis J, Heffron S, **Heald AE**. Effect of protease inhibitors on the sense of taste. *Nutrition* 1999; 15:767-72.
19. Schiffman SS, Zervakis J, Shaio E, **Heald AE**. Effect of the nucleoside analogs zidovudine, didanosine, stavudine and lamivudine on the sense of taste. *Nutrition* 1999; 15:854-9.

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20. Schiffman SS, Zervakis J, Westall HL, Graham BG, Metz A, Bennett JL, **Heald AE**. Effect of antimicrobial and anti-inflammatory medications on the sense of taste. *Physiology & Behavior* 2000; 69:413-24.
21. Currier JS, Williams PL, Koletar SL, Cohn SE, Murphy RL, **Heald AE**, Hafner R, Bassily EL, Lederman HM, Knirsch C, Benson CA, Valdez H, Aberg JA, McCutchan JA, for the AIDS Clinical Trials Group 362 Study Team. Discontinuation of *Mycobacterium avium* complex prophylaxis in patients with antiretroviral therapy-induced increases in CD4+ cell count: a randomized, double-blind, placebo-controlled trial. *Annals of Internal Medicine* 2000; 133:493-503.
22. Whetten-Goldstein K, Nguyen TQ, **Heald AE**. Characteristics of individuals infected with the human immunodeficiency virus and provider interaction in the predominantly rural Southeast. *Southern Medical Journal* 2001; 94:212-22.
23. Koletar SL, **Heald AE**, Finkelstein D, Hafner R, Currier JS, McCutchan JA, Vallee M, Torriani FJ, Powderly WG, Fass RJ, Murphy RL, for the AIDS Clinical Trials Group 888 Study Team. A prospective study of discontinuing primary and secondary *Pneumocystis carinii* prophylaxis after CD4 count increase to $>200 \times 10^6/l$. *AIDS* 2001; 15:1509-15.
24. Von Reyn CF, Williams PL, Lederman HM, McCutchan JA, Koletar SL, Murphy RL, Cohn SE, Evans T, **Heald AE**, Colquhoun D, Bassily EL, Currier JS. Skin test reactivity and cellular immune responses to *Mycobacterium avium* sensitin in AIDS patients at risk for disseminated *M. Avium* infection. *Clinical and Diagnostic Laboratory Immunology* 2001; 8:1277-8.
25. Wellons MF, Sanders L, Edwards LJ, Bartlett JA, **Heald AE**, Schmader KE. HIV infection: treatment outcomes in older and younger adults. *Journal of American Geriatrics Society* 2002; 50:603-7.
26. Szczech LA, Edwards LJ, Sanders LL, van der Horst C, Bartlett JA, **Heald AE**, Svetkey LP. Protease inhibitors are associated with a slowed progression of HIV-related renal diseases. *Clinical Nephrology* 2002; 57:336-41.
27. Villaret D, Glisson B, Kenady D, Hanna E, Carey M, Gleich L, Yoo GH, Futran N, Hung MC, Anklesaria P, **Heald AE**. A multicenter phase II study of tgDCC-E1A for the intratumoral treatment of patients with recurrent head and neck squamous cell carcinoma. *Head & Neck* 2002; 24:661-9.
28. Flotte TR, Zeitlin PL, Reynolds TC, **Heald AE**, Pedersen P, Beck S, Conrad CK, Brass-Ernst L, Humphries M, Sullivan K, Wetzel R, Taylor G, Carter BJ, Guggino WB. Phase I trial of intranasal and endobronchial administration of a recombinant adeno-associated virus serotype 2 (rAAV2)-CFTR vector in adult cystic fibrosis patients: a two-part clinical study. *Human Gene Therapy* 2003; 14:1079-88.
29. Moss RB, Rodman D, Spencer LT, Aitken ML, Zeitlin PL, Waltz D, Milla C, Brody AS, Clancy JP, Ramsey B, Hamblett N, **Heald AE**. Repeated AAV2 aerosol-mediated CFTR gene transfer to the lungs of patients with cystic fibrosis: a multicenter, double-blind, placebo-controlled trial. *Chest* 2004; 125:509-21.

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30. Croteau GA, Martin DB, Camp J, Yost M, Conrad C, Zeitlin PL, **Heald AE**. Evaluation of exposure and health care worker response to nebulized administration of tgAAVCF to patients with cystic fibrosis. *Annals of Occupational Hygiene* 2004; 48:673-81.
31. Giles JT, Mease P, Boers M, Bresnihan B, Conaghan PG, **Heald A**, Maksymowych WP, Maillefert JF, Simon L, Tsuji W, Wakefield R, Woodworth T, Schumacher HR, Bingham CO 3rd. Assessing single joints in arthritis clinical trials. *Journal of Rheumatology* 2007; 34:641-7.
32. Moss RB, Milla C, Colombo J, Accurso F, Zeitlin PL, Clancy JP, Spencer LT, Pilewski J, Waltz DA, Dorkin HL, Ferkol T, Pian M, Ramsey B, Carter BJ, Martin DB, **Heald AE**. Repeated aerosolized AAV-CFTR for treatment of cystic fibrosis: a randomized placebo-controlled phase 2B trial. *Human Gene Therapy* 2007; 18:726-32.
33. Mehendale S, van Lunzen J, Clumeck N, Rockstroh J, Vets E, Johnson PR, Anklesaria P, Barin B, Boaz M, Kochhar S, Lehrman J, Schmidt C, Peeters M, Schwarze-Zander C, Kabamba K, Glaunsinger T, Sahay S, Thakar M, Paranjape R, Gilmour J, Excler JL, Fast P, **Heald AE**. A phase 1 study to evaluate the safety and immunogenicity of a recombinant HIV type 1 subtype C adeno-associated virus vaccine. *AIDS Research and Human Retroviruses* 2008; 24:873-80.
34. Mease PJ, Hobbs K, Chalmers A, El-Gabalawy H, Bookman A, Keystone E, Furst DE, Anklesaria P, **Heald AE**. Local delivery of a recombinant adeno-associated vector containing a tumor necrosis factor- α antagonist gene in inflammatory arthritis: a phase 1 dose-escalation safety and tolerability study. *Annals of Rheumatic Diseases* 2009; 68:1247-54.
35. Keen HI, Bingham CO 3rd, Bradley LA, Conaghan PG, **Heald AE**, Kaeley GS, Maksymowych WP, Moskowitz RW, Schumacher HR Jr, Woodworth TE, Mease PJ. Assessing single joints in arthritis clinical trials. *Journal of Rheumatology* 2009; 34:2092-6.
36. Mease PJ, Wei N, Fudman EJ, Kivitz AJ, Schechtman J, Trapp RG, Hobbs KF, Greenwald M, Hou A, Bookbinder SA, Graham GE, Wiesenhutter CW, Willis L, Ruderman EM, Forstot JZ, Maricic MJ, Dao KH, Pritchard CH, Fiske DN, Burch FX, Prupas HM, Anklesaria P, **Heald AE**. Safety, tolerability and clinical outcomes after intra-articular injection of a recombinant adeno-associated vector containing a TNF antagonist gene: results of a phase 1/2 study. *Journal of Rheumatology* 2010; 37:692-703.
37. **Heald AE**, Fudman EJ, Anklesaria P, Mease PJ, on behalf of the 13G01 Study Team. Single joint outcome measures: preliminary validation of patient-reported outcomes and physical examination. *Journal of Rheumatology* 2010; 37:1042-8.
38. Vardas E, Kaleebu P, Bekker L-G, Hoosen A, Chomba E, Johnson PR, Anklesaria P, Birungi J, Barin B, Boaz M, Cox J, Lehrman J, Stevens G, Gilmour J, Tarragona T, Hayes P, Lowenbein S, Kizito E, Fast P, **Heald AE**, Schmidt C. A phase 2 study to evaluate the safety and immunogenicity of a recombinant HIV-1 vaccine based on adeno-associated virus. *AIDS Research and Human Retroviruses* 2010; 26:933-42.
39. Bucher JB, Golden MR, **Heald AE**, Marra CM. Stroke in a patient with human immunodeficiency virus and syphilis treated with penicillin and antiretroviral therapy. *Sexually Transmitted Diseases* 2011; 38:442-4.

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40. Schmidt C, Smith C, Barin B, Bakhtyari A, Bart PA, Bekker LG, Chomba E, Clumeck N, Ho D, Hoosen A, Jaoko W, Kaleebu P, Karita E, Keefer MC, van Lunzen J, McMichael A, Mehendale S, Peters B, Ramanathan V, Robinson A, Rockstroh J, Vardas E, Vets E, Weber J, Graham BS, Than S, Excler JL, Kochhar S, Ho M, **Heald A**, Fast PE. Background morbidity in HIV vaccine trial participants from various geographic regions as assessed by unsolicited adverse events. *Human Vaccines & Immunotherapeutics* 2012; 8:630-8.
41. **Heald AE**, Iversen PL, Saoud JB, Sazani P, Charleston JS, Axtelle T, Wong M, Smith WB, Vutikullird A, Kaye E. Safety and pharmacokinetic profiles of phosphorodiamidate morpholino oligomers with activity against Ebola virus and Marburg virus: results of two single ascending dose studies. *Antimicrobial Agents and Chemotherapy* 2014; 58:6639-47.
42. Warren TK, Whitehouse CA, Wells J, Welch L, **Heald AE**, Charleston JS, Sazani P, Reid SP, Iversen PL, Bavari S. A single phosphorodiamidate morpholino oligomer targeting VP24 protects rhesus monkeys against lethal Ebola virus infection. *MBio* 2015; 6:e02344-14.
43. **Heald AE**, Charleston JS, Iversen PL, Warren TK, Saoud JB, Al-Ibrahim M, Wells J, Warfield KL, Welch LS, Sazani P, Wong M, Berry B, Kaye E, Bavari S. AVI-7288 for Marburg virus in nonhuman primates and humans. *New England Journal of Medicine* 2015; 373:338-48.
44. Warren TK, Whitehouse CA, Wells J, Welch L, Charleston JC, **Heald A**, Nichols DK, Mattix ME, Palacios G, Kugleman JR, Iversen PL, Bavari S. Delayed time-to-treatment of an antisense morpholino oligomer is effective against lethal Marburg virus infection in cynomolgus macaques. *PLoS Neglected Tropical Diseases* 2016; 10:e0004456.