

**RECOMBINANT DNA
ADVISORY COMMITTEE
TO BE OR NOT TO BE**

**CROI COMMUNITY CURE WORKSHOP
FEBRUARY 21, 2016**

THE RAC: TO BE OR NOT TO BE

- RECOMBINANT DNA ADVISORY COMMITTEE (RAC)
- NIH REQUESTS INSTITUTE OF MEDICINE (IOM) RAC REVIEW
- IOM REPORT ON THE FUTURE ROLE OF RAC REVIEW
- RAC REVIEW OF VORINOSTAT + AGS-004
- COMMUNITY RAC ACTION
- THE FATE OF VORINISTAT + AGS-004

THE RAC: TO BE OR NOT TO BE

- THE RAC: INSTITUTED IN 1974
 - OVERSIGHT OVER NEW RECOMBINANT DNA TECHNOLOGY
 - TRANSFER OF GENETIC MATERIALS INTO HUMANS
 - TO REPLACE OR COMPENSATE FOR ABNORMAL GENES
 - TO ENHANCE IMMUNE SYSTEM TO FIGHT CANCER
 - FRANCIS COLLINS REQUESTED IOM RAC REVIEW-2013

THE RAC: TO BE OR NOT TO BE

- RAC REVIEW QUESTIONS

- DOES HUMAN GENE TRANSFER RESEARCH RAISE SPECIAL ISSUES THAT WARRANT CONTINUING EXTRA OVERSIGHT?

- SAME LEVEL OF CONCERN IS NOT PRESENT TODAY AFTER HUNDREDS OF CLINICAL TRIALS HAVE EVALUATED SAFETY AND EFFECTIVENESS

- IOM REPORT CONCLUDES THAT RAC OVERSIGHT IS ARGUABLY OVERLAPPING AND REDUNDANT IN LIGHT OF FDA AND IRB REVIEW

THE RAC: TO BE OR NOT TO BE

- DIRECTOR COLLINS REQUIRES CONDITIONS FOR RAC REVIEW- 2014:
 - REVIEW CANNOT BE ADEQUATELY CONDUCTED BY FDA, IRBS, ETC.
- AND
- ONE OR MORE OF THE FOLLOWING CRITERIA ARE PRESENT:
 - NEW VECTOR, GENETIC MATERIAL OR FIRST-IN-HUMAN DELIVERY METHOD
 - PRECLINICAL SAFETY DATA OBTAINED USING NEW UNKNOWN AND UNCONFIRMED PRECLINICAL MODEL SYSTEM
 - POSSIBLE TOXICITIES THAT ARE NOT WIDELY KNOWN

THE RAC: TO BE OR NOT TO BE

○ RAC REVIEW vs A RAC PUBLIC HEARING

○ EXPEDITED REVIEW CAN BE CONDUCTED QUICKLY WITHOUT THE NEED FOR A PUBLIC HEARING

○ PUBLIC HEARING REQUIRES APPROXIMATELY FOUR EXTRA MONTHS BASED ON QUATERLY RAC MEETING SCHEDULE

THE RAC: TO BE OR NOT TO BE

- **VORINISTAT + AGS-004 (DAVID MARGOLIS & CYNTHIA GAY, UNC)**
 - **PHASE I STUDY MEASURING THE POTENTIAL AGS-004 + VORINOSTAT (VOR)**
 - **WILL A COMBINATON OF SERIAL AGS-004 VACCINATIONS AND VOR RESULT IN A DEPLETION OF PERSISTENT, LATENT HIV INFECTION?**
 - **N= 12 HIV+ MEN/WOMEN, ≥ 18 , ON STABLE cART, SUPPRESSED FOR ≥ 2 YEARS WITH CD4s ≥ 300 , FOLLOWED UP TO 96 WEEKS**
 - **PATIENTS WITH MEASUREABLE INCREASES IN HIV RNA EXPRESSION FREQUENCY IN CD4+ CELLS EXPOSED EX VIVO TO VOR WILL PROCEED TO THE ACTIVE PHASE OF THE STUDY AND WILL RECEIVE MULTIPLE DOSES OF VOR + AGS-004.**

THE RAC: TO BE OR NOT TO BE

- RAC REQUIRED PUBLIC HEARING
- OCCASIONED A FOUR MONTH DELAY
- PATIENT ENROLLMENT MILESTONE WAS MISSED
- FUNDING DELAYS RESULTED
- NEW COLLINS CONDITIONS FOR REVIEW NOT PRESENT
- NO GENE MODIFICATION PRESENT
- UNNECESSARY DELAYS SLOW RESEARCH
- ADVERSELY AFFECTS PEOPLE WITH HIV

THE RAC: TO BE OR NOT TO BE

- COMMUNITY ACTION

 - TESTIMONY AT RAC HEARING

 - MDC CAB LETTER TO RAC EXEC SECRETARY LYRIC JORGENSON

 - COLLINS CRITERIA BE REQUIRED FOR PUBLIC HEARINGS

 - MAJORITY RAC VOTE FOR A PUBLIC HEARING

THE RAC: TO BE OR NOT TO BE

- REPLY FROM DR. JORGENSEN: 1-11-2016
 - NIH IS STREAMLINING THE RAC PROCESS
 - NIH IS CURRENTLY ANALYZING FEDERAL REGISTER COMMENTS
 - NIH WILL PUBLISH FINAL POLICY IN THE NEXT SEVERAL MONTHS

THE RAC: TO BE OR NOT TO BE

- THE FATE OF THE VORINOSTAT + AGS-004 PROTOCOL:
 - MORE DATA REQUESTED AT 12-4-15 PUBLIC HEARING
 - SPONSOR FELT QUESTIONS POSED WERE ALREADY ANSWERED
 - FINAL 12-17-15 RAC LETTER MADE SEVERAL VERY SIMPLE RECOMMENDATIONS RE: QC OF TRANSFERRED RNA AND IC.
 - OK FROM DAIDS ON 2-8-16 TO ENROLL THE FIRST PATIENT

THE RAC: TO BE OR NOT TO BE

○ THANKS

○ JEFF SHEEHY, MDC CARE CAB

○ DAVE MARGOLIS AND CYNTHIA GAY, UNC

○ HANS-PETER KIEM, FHCRC SEATTLE & RAC CHAIR