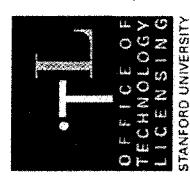


Stanford University
Office of Technology Licensing

Stanford wishes to offer a license
to its invention entitled:
“PCR Assays for Monitoring
Antiviral Therapy and Making
Therapeutic Decisions in the
Treatment of AIDS”

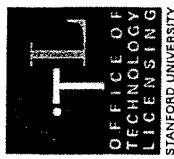
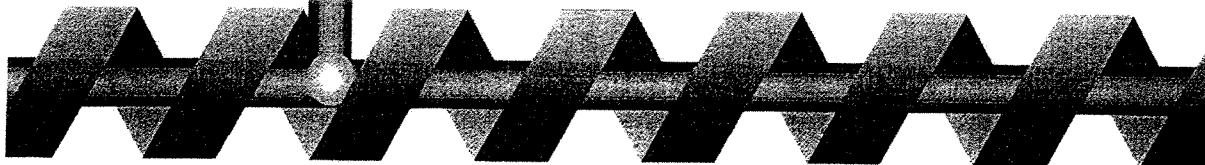


STAN 029325

Confidential –
Attorneys' Eyes Only

Outline

- Why is Stanford Interested in Licensing This Technology to Roche?
- Background of Technology
- What is Stanford Offering?
- The Offer
- Next Steps



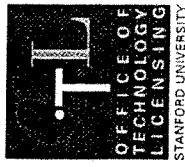
Confidential –
Attorneys' Eyes Only STAN 029326

Why Roche?

- Stanford and Roche have had a long and fruitful relationship
- Although other companies might have an interest, we believe that Roche would be the best partner for Stanford for the subject Stanford IP

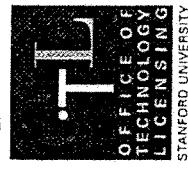
Confidential –
Attorneys' Eyes Only

STAN 029327



Background of Technology

- During the early 1990's, Dr. Mark Holodniy working under Dr. Merigan with support from Dr. Katzenstein studied DNA in cells for a possible diagnostic of HIV
- Cetus Scientists were working on DNA as a diagnostic test
- Refer to UCSF/Cetus article "Risk of HIV-1 in Screened Blood Donations" The New Eng. J. of Medicine, Vol. 325, No. 1 Pp. 1-5



Confidential –
Attorneys' Eyes Only STAN 029328

Background of Technology

- Meanwhile at Stanford, studies were being conducted on RNA in plasma for a possible diagnostic and quantification of HIV following therapy
- Refer to Stanford/Cetus article "Detection and Quantification of HIV RNA in Patient Serum by Use of PCR," in **The Journal of Infectious Diseases**, April 1991 Pp. 862-866

5



Confidential –
Attorneys' Eyes Only STAN 029329

Background of Technology

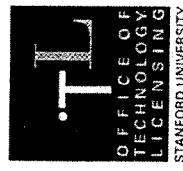
- Refer to Stanford article "Reduction in Plasma Human Immunodeficiency Virus Ribonucleic Acid after Dideoxynucleoside Therapy as Determined by PCR", JCI 88:1755-1759, 1991



STAN 029330
Confidential –
Attorneys' Eyes Only

Background of Technology

- The value of quantification of HIV RNA in plasma serum was not evident to Cetus at that time or through June 1992
- Refer to "Detection of Human Retroviruses by PCR," in Annals of Medicine, June 1992 Pp. 211-214
- Cetus subsequently explored detection of proviral DNA in PBMCs and various tissues

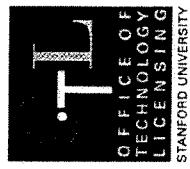


Confidential –
Attorneys' Eyes Only

STAN 029331

Background of Technology

- However, Dr. Holodniy, Dr. Katzenstein and Dr. Merigan had conceived that measurement of HIV RNA from plasma could be used for assessing efficacy of antiviral therapy
- Refer to Stanford article “Reduction in Plasma Human Immunodeficiency Virus Ribonucleic Acid after Dideoxynucleoside Therapy as Determined by PCR”, JCI 88:1755-1759, 1991



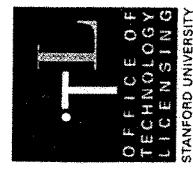
Confidential –
Attorneys' Eyes Only

STAN 029332

Background of Technology

- Follow on work at Stanford showed that the test could be ultra-sensitive. This presented an opportunity to provide a test that could be used by every patient to monitor therapy
- Refer to Stanford article "Biological Variation and Quality Control of Plasma RNA Quantitation by RT PCR" JCM, vol. 31:2960-2966, 1993

9



Confidential –
Attorneys' Eyes Only STAN 029333

Background of Technology

- Dr. Merigan's, Dr. Katzenstein's and Dr. Holodniy's work resulted in the issuance of U.S. Patent No. 5,968,730, among others
- Continuations based on the same application "family" remain pending

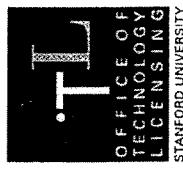


Confidential –
Attorneys' Eyes Only

STAN 029334

What are we offering? Stanford's IP:

- A method for evaluating the effectiveness of anti-HIV therapy of a patient:
 - collecting a plasma sample from an HIV-infected patient who is being treated with an antiretroviral agent;
 - amplifying the HIV-encoding nucleic acid in the plasma sample using HIV primers in about 30 cycles of PCR; and
 - testing for the presence of HIV-encoding nucleic acid, in the product of the PCR;
- in which the absence of detectable HIV-encoding nucleic acid correlates positively with the conclusion that the antiretroviral agent is therapeutically effective. See U.S. Patent No. 5,968,730, Claim 1

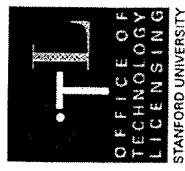


Confidential –
Attorneys' Eyes Only STAN 029335

Stanford's IP (cont.)

- Collecting a plasma sample from an HIV-infected patient who is being treated with an antiretroviral agent
 - quantification of viral load in human plasma
 - assessment of patient prognosis
 - monitoring of effect of concurrent antiretroviral therapy
 - useful in clinical management of HIV infected patients

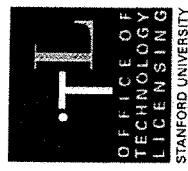
12



Confidential –
Attorneys' Eyes Only STAN 029336

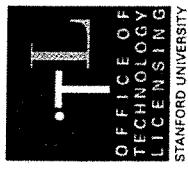
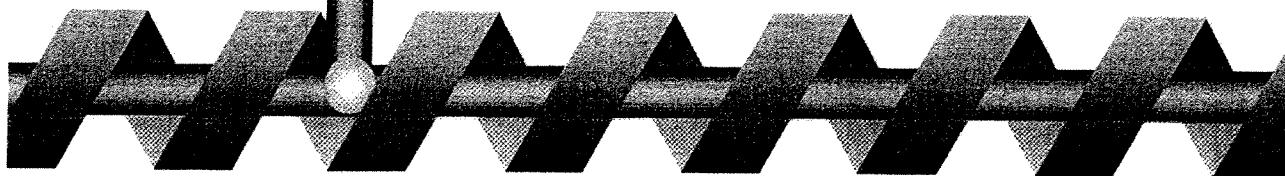
Stanford's IP (cont.)

- Amplifying the HIV-encoding nucleic acid in the plasma sample using HIV primers in about 30 cycles of PCR
 - PCR assay of plasma HIV RNA
 - Use of HIV primers about 20-30 bases long



Stanford's IP (cont.)

- Testing for the presence of HIV-encoding nucleic acid, in the product of the PCR
 - quantification of nucleic acid by hybridizing product of PCR with detectably labeled probe that is complementary to the HIV sequence
 - amount of signal generated by probe hybridized to PCR product can be compared to amount of signal generated by probe hybridized to a known copy number of HIV, e.g., by using a microwell plate reader



Confidential –
Attorneys' Eyes Only
STAN 029338

Stanford's IP (cont.)

- The absence of detectable HIV-encoding nucleic acid correlates positively with the conclusion that the antiretroviral agent is therapeutically effective
 - decreased nucleic acid copy number correlates with effective therapy
 - increased nucleic acid copy number correlates with disease progression

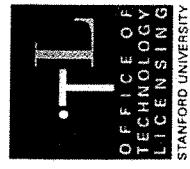


Confidential –
Attorneys' Eyes Only
STAN 029339

The Offer

- Stanford wishes to extend to Roche an offer to obtain an Exclusive License to the subject Stanford IP
REDACTED
- License would include rights to patents that may issue based on pending applications from same patent "family"
- Stanford inventors Drs. Merigan, Holodniy and Katzenstein would be available to collaborate with Roche Scientists

16



Confidential –
Attorneys' Eyes Only
STAN 029340

The Offer (cont.))

- The license will contain other terms and conditions normally found in Stanford's licenses and reasonably acceptable to Roche
- The offer extended hereunder is valid until May 31, 2000, unless withdrawn prior to that date
- No license or other rights are implied by this document

17

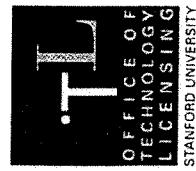


Confidential –
Attorneys' Eyes Only
STAN 029341

Next Steps

- Terms and conditions would be negotiated in good faith within 90 days of Stanford's receipt of Roche's written acceptance
- We look forward to continuing our relationship through a mutually acceptable license agreement to this technology

18



Confidential –
Attorneys' Eyes Only
STAN 029342