



**“Science Improving Health”**

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**Clone 3 Human Monoclonal Antibody**  
**Neutralizing Effect on HIV**  
**2017**

**[www.bioclonetics.com](http://www.bioclonetics.com)**

**For Recipient Only**

# Who We Are

BioClonetics Immunotherapeutics is a biotechnology company with a proprietary methodology and expertise for creating cell lines that produce fully human IgG1 monoclonal antibodies for the treatment of HIV/AIDS and other infectious diseases.

From this technology, we have created proprietary cell lines that produce a fully human monoclonal antibody (called Client 3) that targets and neutralizes HIV. The company has also produced monoclonal antibodies that can be used to treat influenza, tetanus, rabies and diphtheria.

# The Problem

## The Problem:

- 36.9 million individuals have HIV worldwide.
- Over 2 million people are newly infected each year and 1.2 million die each year.
- Approximately 700 new infections occur daily through maternal to child transmission (MTCT).
- In North America, 1.4 million individuals are infected with HIV annually and over 87,000 are newly infected each year.
- Those infected by HIV are primarily treated with anti-retroviral (ARV) chemotherapy drugs that only suppress the symptoms of the virus and can cause severe injury to critical body organs.

# The Solution

## The Solution:

- The Company's Clone 3 monoclonal antibody is effective against all:
  - U.S., European and South American strains of the HIV virus
  - Including those strain identified as drug-resistant to antiretrovirals (ARVs)
- The antibody is non-toxic, provides an immunotherapeutic and safe treatment option and is more affordable than ARVs.
- The cell line that produced Clone 3 is proprietary and intellectual property is owned by the company.

## How Clone 3 Antibody Was Discovered

At the outset of the AIDS epidemic in the early to mid 1980's, the founder of BioClonetics, Dr. Joseph Cotropia, M.D., treated numerous HIV positive patients in his medical practice. In treating these patients, he recognized that some, while having the virus, did not progress to frank AIDS but rather were able to naturally fend off the virus.

Dr. Cotropia theorized and later confirmed that these patients were a small subset of HIV patients (today called "long-term nonprogressors") who naturally carry antibodies that control the virus. Using what is now a company proprietary technique invented by Dr. Cotropia, he cloned the repertoire of B cells of these patients and isolated several clones that were producing antibodies that would bind to the virus.

## How Clone 3 Antibody Works

These antibodies were then tested against HIV isolates (strains of the virus) and one antibody was found to remarkably neutralize 37 of 41 strains of the virus against which it was tested. Dr. Cotropia also identified the location on the virus to which the antibody binds and found that that location is immutable (never changing) in over 98% of all 4,000 different global strains of HIV. This means that Dr. Cotropia had found an antibody that binds to and thus neutralizes the virus by binding to a stable portion (called the gp41 epitope binding site). The binding of the antibody to the virus at this location results in the virus not being able to bind to and infect the human CD4+ cells.

The immutability of the target site on the virus provides the basis on which a vaccine can be produced for HIV prevention.



# PROOF Of Efficacy

Clone 3 has been tested against 45 strains of the virus at these 5 independent research institutions :

1. University of California, San Francisco, CA, USA (Jay Levy, MD)
2. University of South Florida, Tampa, FL, USA (Kenneth Ugen, PhD)
3. University of Vienna, Polymun Scientific, GmbH, Vienna, AUSTRIA, (Hermann Katinger, PhD)
4. Duke University, Durham, NC, USA (David Montefiori, PhD)
5. Harvard University, Dana Farber Cancer Institute, Boston, MA, USA, (Ruth Ruprecht, MD, PhD)

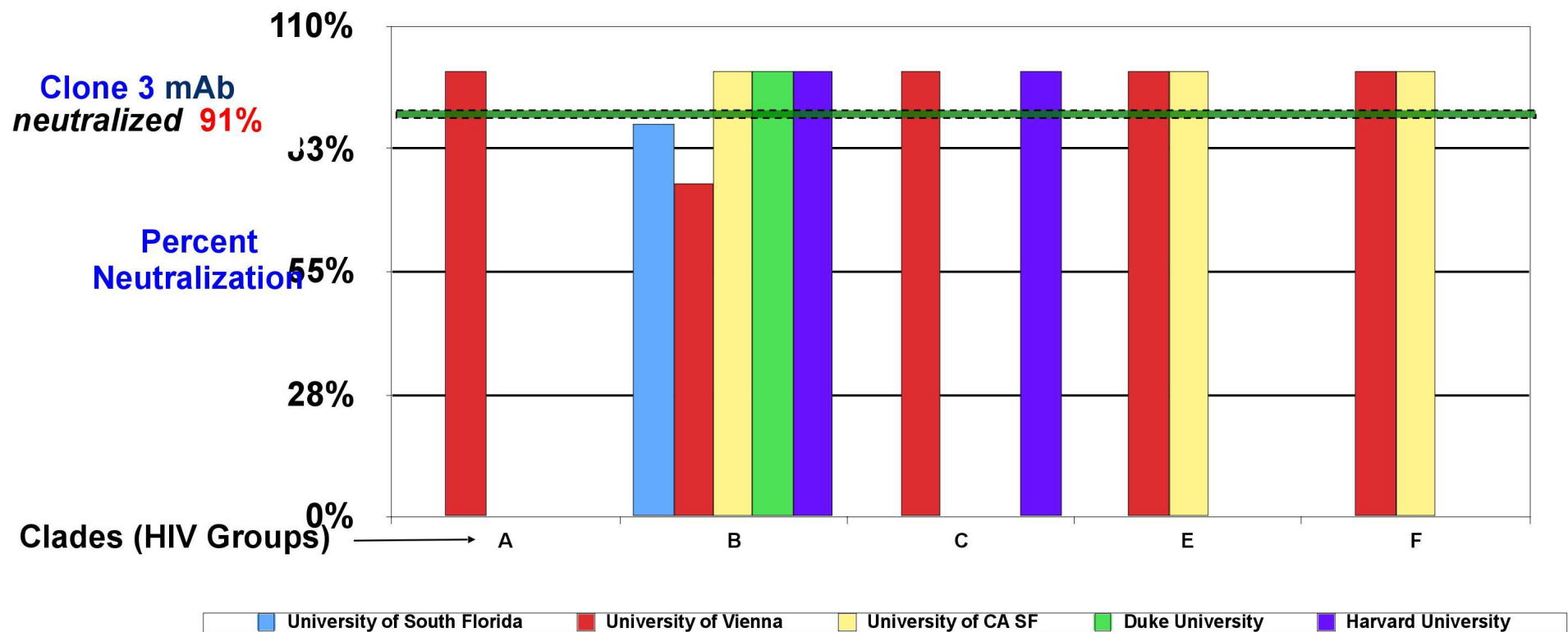
Results of these *in-vitro* neutralization tests of Clone 3 show over 91% of the HIV viruses tested to be neutralized.

The Clone 3 fully human antibody neutralized HIV in all clades and groups found around the world.

# PROOF Of Efficacy – 3<sup>rd</sup> Party Evidence

## Independent Laboratory Test Results

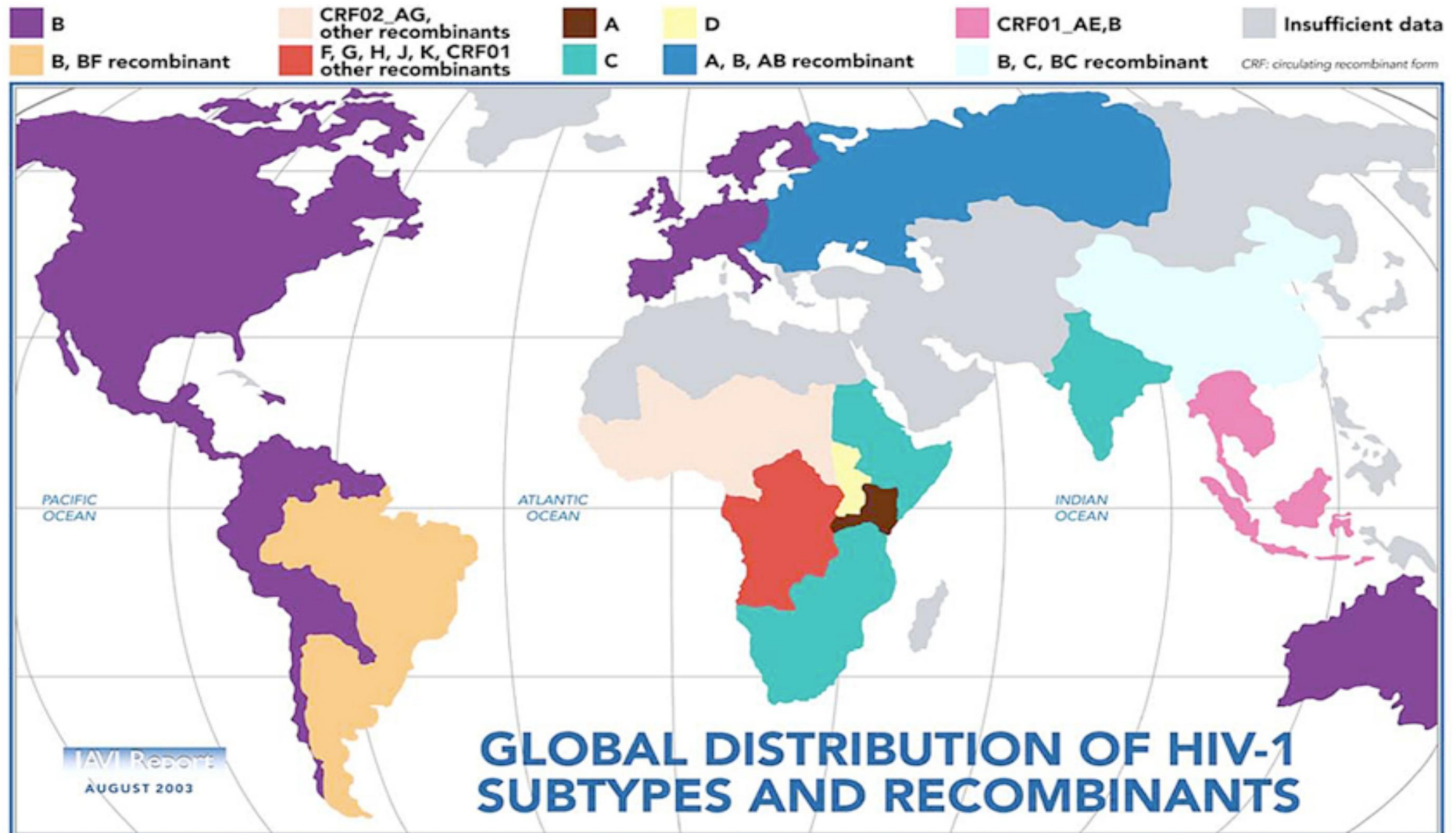
- Test in five (5) international research institutes have shown that **Clone 3** antibody *neutralizes* (at IC90\*) **41 of 45 (over 91%)** of primary HIV viruses tested, from clades (HIV Groups) A, B, C, E, and F from around the globe



\* IC90 - Inhibitory Concentration of Clone 3 mAb (<30 microgram/ml) that *neutralizes* 90% of HIV virions



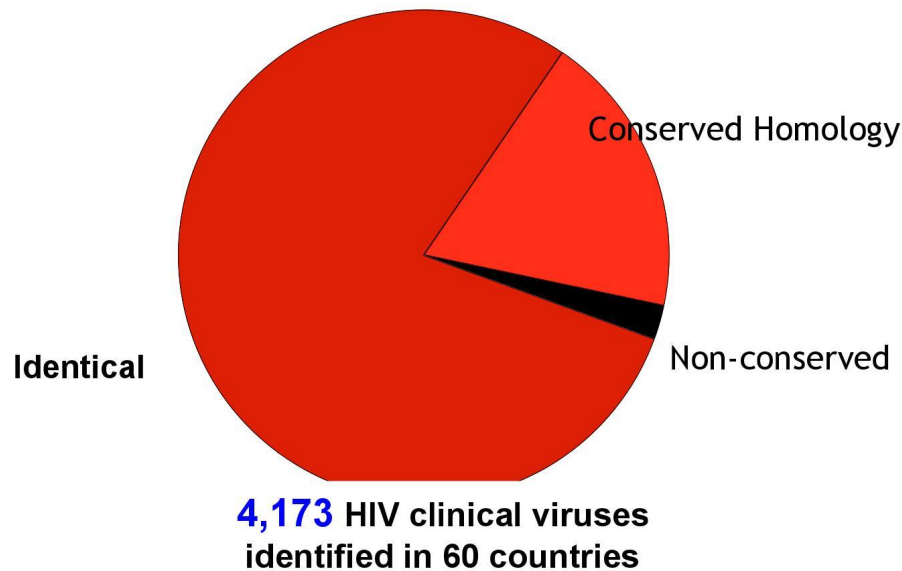
**Clone 3 Antibody** has GLOBAL application by neutralizing HIV clades A, B, C, E, and F that exist around the world.



Source: Francine E. McCutchan, Henry M. Jackson Foundation (Rockville, Maryland). McCutchan and colleagues are indebted to the many international collaborators who helped develop the data used to generate this map.

# Clone 3 can be expected to neutralize 98% of all HIV viral strains.

The HIV target KLIC site  
*neutralized* by Clone 3 exists in  
**98%** of all known HIV viral  
strains.



- **Clone 3** Antibody targets **98%** of all HIV viral strains worldwide, via epitope KLIC
  - (i) Exact match [KLIC] on viral target: **78%**
  - (ii) Conservative match on viral target: **20%**
- Mis-match: **2%**
- **RED = DEAD HIV**

• Viral Database; 16 February 2016

[http://www.hiv.lanl.gov/content/immunology/ab\\_search?results=Search&ab\\_id=771](http://www.hiv.lanl.gov/content/immunology/ab_search?results=Search&ab_id=771)

[http://www.hiv.lanl.gov/cgi-bin/QUICK\\_ALIGNv2/convent.cgi?seq\\_input=epitope%09KLIC&nucpro=pro](http://www.hiv.lanl.gov/cgi-bin/QUICK_ALIGNv2/convent.cgi?seq_input=epitope%09KLIC&nucpro=pro)

# Completed Steps

## Completed Work

- Isolating and cloning of B cells of HIV patients to create monoclonal antibodies.
- Screening of antibodies to identify Clone 3.
- *In vitro* testing of Clone 3 against HIV strains to confirm neutralizing capability.
- Identification of the binding site of Clone 3 on the HIV virus.
- Fully sequenced the light chain protein and heavy chain protein that programs for the full Clone 3 mAb molecule.

# Next Steps

## Next Steps

- Pharmaceutically produce Clone 3 in a form (called the "recombinant" antibody) that will ultimately be used in the treatment of patients – this is accomplished using a known procedure through isolation of corresponding DNA from the parent cell line genomic blueprint which encodes to produce the existing monoclonal antibody and inserting the genetic code into a fast producing and FDA approved cell line.
- Testing the recombinant antibody against a full panel of HIV isolates and then in animal trials and human trials -- leading to patient application.

# Management Team

## Executives

- Joseph Cotropia, MD, MS, President & Chief Science Officer
- Charles S. Cotropia, JD, General and Patent Counsel
- Dimiter Ivanov Dentchev, MD, PhD, Senior Research Physician
- Tomasz H. Zastawny, DSc, PhD, Chief Operations Officer
- Paul D. Fellegly, Chief Financial Officer

## Advisors

- Gaurav, Chandra MD, FAGE, MBA, MRCS
- Seth A. Sheiner, MD, MSIS, CPHIMS
- Ellen S. Vitetta, PhD
- Yvonne J. Bryson, MD
- Dalila B. Corry, MD



# Intellectual Property

- Patent application for “Anti-HIV small molecular peptide” covers the use of small molecules for interrupting and preventing binding between the HIV virus and the CD4+ cell using blocking peptides and/or competitive peptides.
- Clone 3 Cell Line that produces the fully human antibody that specifically targets and neutralizes the HIV virus is proprietary. This specific cell line is necessary to create the clinical anti-HIV passive immunotherapy and potential anti-HIV vaccine.
- The Company proprietary mAb methodologies & immunotherapeutic technologies platform will be used to create monoclonal antibodies for treatment of viral infectious diseases against numerous infectious diseases.



# Company Present Strategies

## Strategy Options:

- Develop and test and then license the Clone 3 immunotherapeutic technologies platform to Big Pharma
- License the proprietary development technology for creating fully human neutralizing monoclonal antibodies
- Develop the Clone 3 through full commercialization with a limited number of key investors

# Summary

## **Large unmet medical need**

- Current chemotherapeutic ARV drugs can not eradicate HIV from patients entirely; therefore, they can not provide a therapeutic cure.
- Pipeline drugs and trial vaccines have not been shown to be effective or protective to those to whom they have been administered.

## **BioClonetics' proprietary antibody-based immunotherapeutic technologies platform**

- Targets highly conserved amino acid sequences (epitope) on HIV's viral envelope that are functionally required for HIV to replicate.

[www.bioclone.com](http://www.bioclone.com)

**Find out more at**

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