



Novel Concept of Dendrimers

*Presented by
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VivaGel' – Downsizing Microbicides



Explosion of new knowledge relating to HIV is so rapid, that any information would be out of date by the time of it's release. Nevertheless, should be asserted, that modern plague is capable to diminish average life expectancy in 38 countries since 1999, not only in underdeveloped, but in industrialized nations[The Global Fund, "The Status and Impact of the Three Diseases: HIV/AIDS," p. 3.]

The background is a collage of images. On the left, a person in a dark suit holds a golden theatrical mask. In the center, a large, dark red bottle is visible. On the right, a person in a red jacket holds another golden theatrical mask. The overall color palette is dominated by reds, oranges, and browns. A semi-transparent white text box is centered over the image.

*‘VivaGel’ – Downsizing
Microbicides*



Worldwide over 7,000
women become
infected with
HIV every day

The most dramatic is that majority of patients are of younger age and incidence of HIV in women is predominated. Not surprisingly, AIDS in females is caused by male intravenous drug abuser partners.

European Study Group on Heterosexual Transmission of HIV submitted results, confirming that spread of infection male-to-female twofold exceeds female-to-male incidence rate. This evidence is far more important among African dwellers, as well other nations.

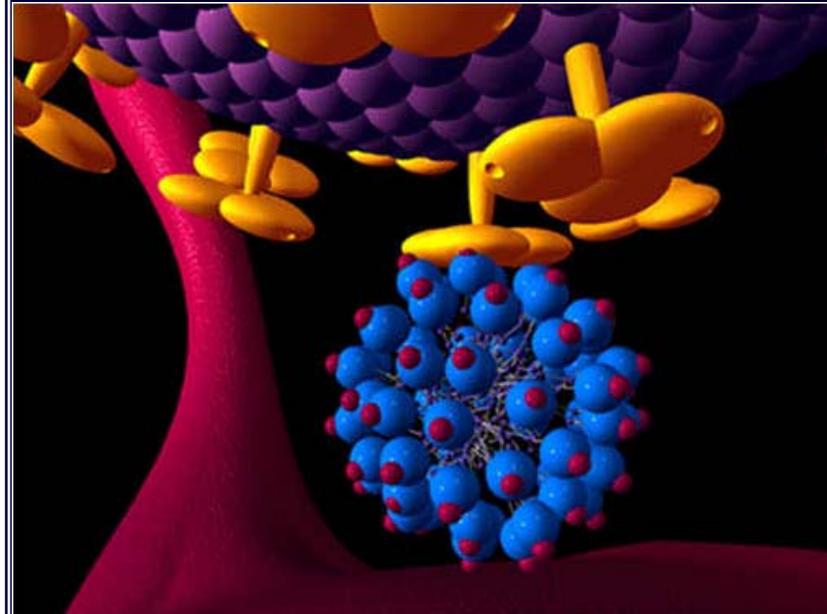
In 2005 the US National Institute of Health (NIH) awarded Starpharma US\$20.3 million to support the development of VivaGel for the prevention of HIV. In April 2006 the US NIH announced it would fund a clinical trial to test the use of VivaGel in the prevention of genital herpes. Anti-HIV microbicides are a target of opportunity for DENDRIMERS. VivaGel is the first DENDRIMER – already proceeding through the FDA approval process and is now being tested around the world in various populations, as one of the vaginal microbicides [“VivaGel Could Cure Starpharma’s Stock,” Forbes/Wolfe Nanotech Report, Vol. 5, No. 6, June 2006, pp. 1-2.]

Some health promoting organizations advocate the development of microbicides because they could put safe, affordable and accessible protection into the hands of women.[See for example, “Global Campaign for Microbicides,” www.global-campaign.org]

Starpharma's dendrimer-based anti-HIV microbicide, VivaGel, goes through clinical trials.

All the microbicide candidates attack GP120 and try to gum up the works enough to prevent binding. But VivaGel stands out as more effective because the many-taloned polyvalent dendrimer is able to stick to HIV at multiple points simultaneously.

The active ingredient in VivaGel works like molecular velcro – inactivating HIV and genital herpes viruses by binding with receptors on the virus's surface and preventing it from attaching to the host cells it is trying to infect. Yes. It's those dendrimer appendages.



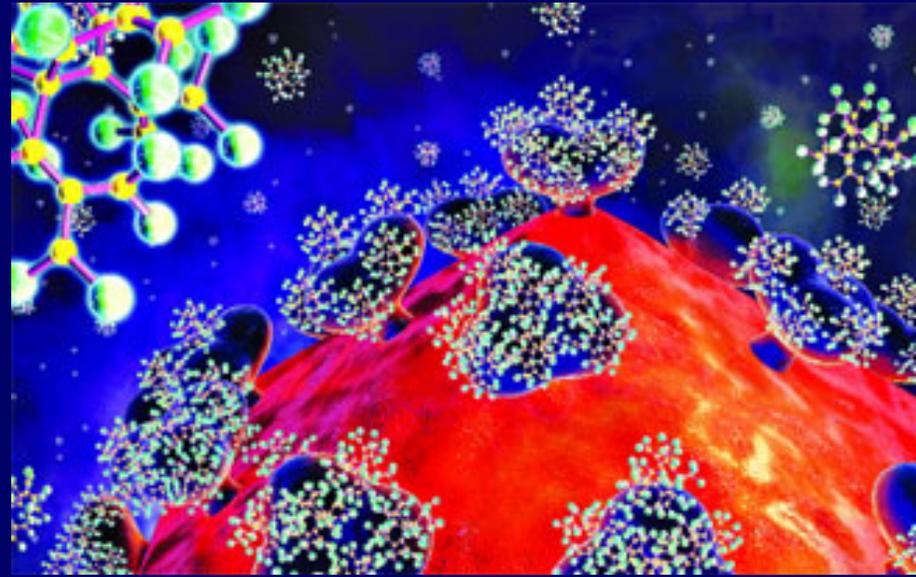
Target for these new microbicides is a protein called GP120, which acts as a kind of docking clamp for HIV, seeking out and binding to healthy cells.

U.S. Food and Drug Administration gives its anticipated 2009 or 2010 approval to the first dendrimer-based pharmaceutical VivaGel.

The dendrimer is not a passive nanoscale material just waiting to bump into its target.

The dendrimer's tendrils are engineered to seek out and neutralize specific areas of HIV, working in a coordinated attack at various points.

That's why Donald Tomalia's invention is finally proving itself, by performing much better than other microbicides undergoing clinical trials in the fight against HIV in the developing world.



“History of the Discovery of Dendrimers”

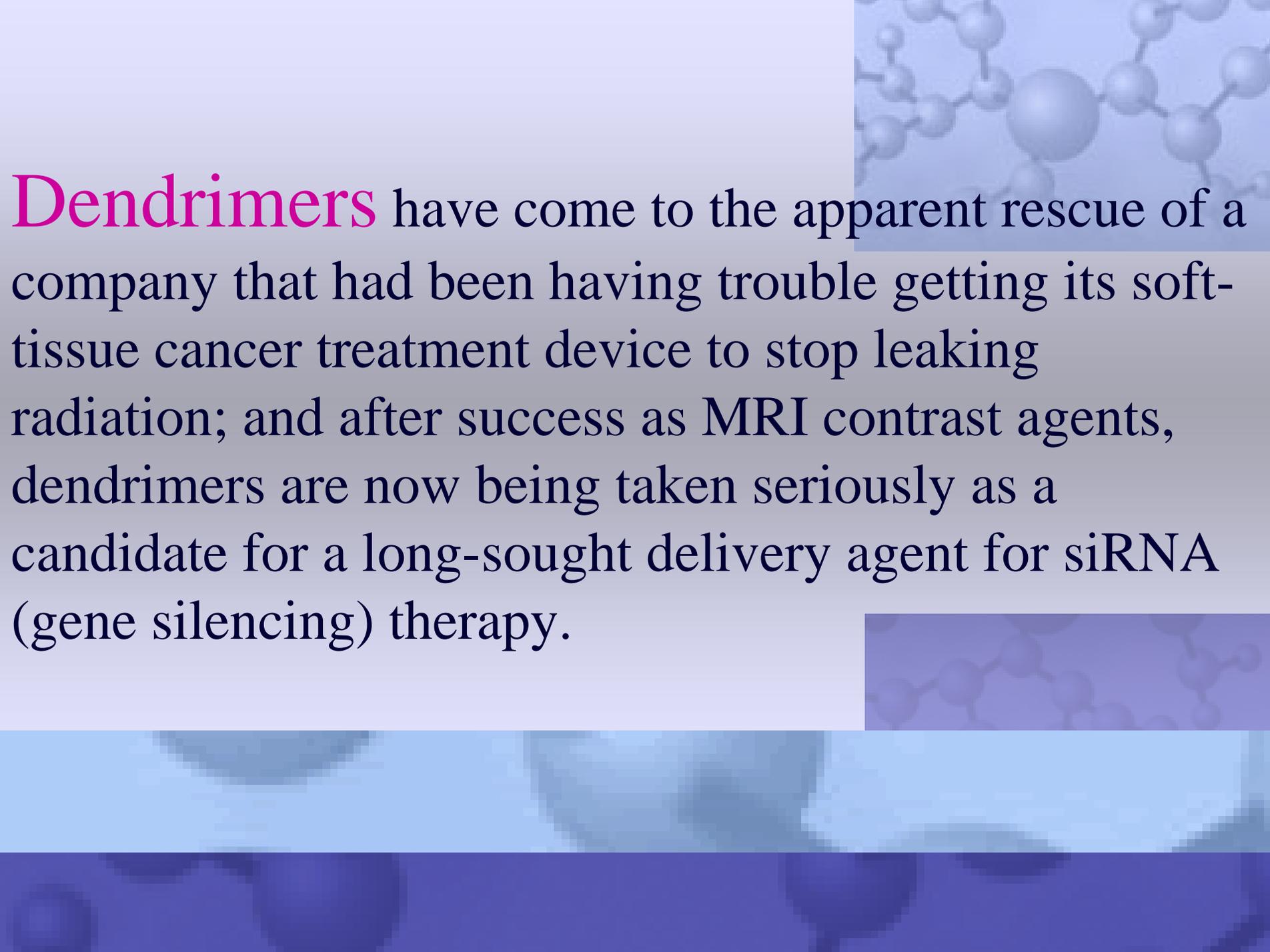
In 1978

NANOTECHNOLOGY PIONEERS

Fritz Vögtle, German scient from the University of Bonn, and just few months aftermath by **Donald A. Tomalia**, who worked for Dow Chemical Co. in Midland, Michigan. almost simultaneously and independently from each other initially reported...

...the concept of Dendrimers.

Thus has a solid theoretical basis for nearly for at least current three decades. This is also the time period, while an invention may go off patent. It is time for some companies try to find ways using soon-to-be-off patent IP in new applications.

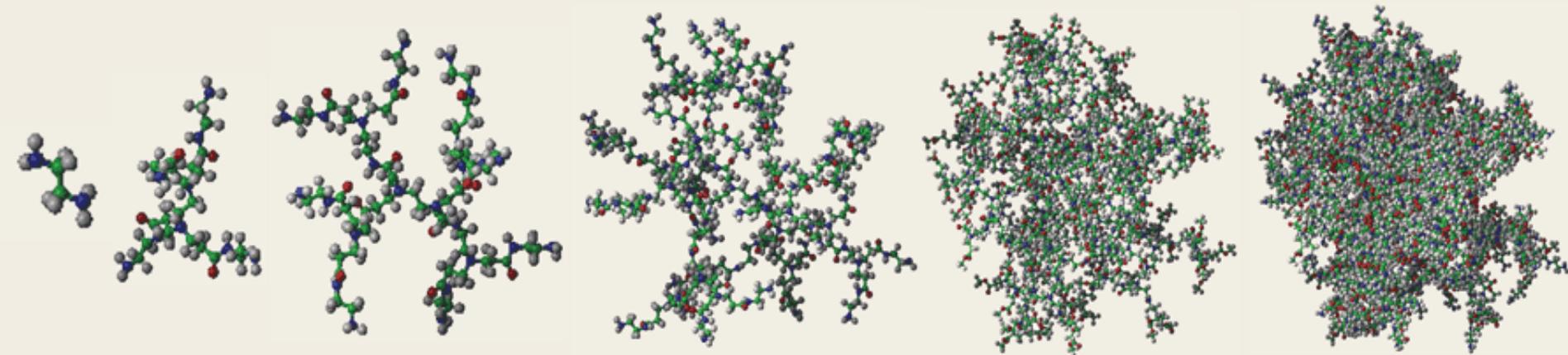
The background features a light blue gradient with faint, semi-transparent molecular models and dendrimer-like structures. A prominent dendrimer is visible in the lower half of the image, rendered in a darker blue. The text is overlaid on the upper portion of the slide.

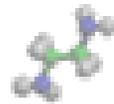
Dendrimers have come to the apparent rescue of a company that had been having trouble getting its soft-tissue cancer treatment device to stop leaking radiation; and after success as MRI contrast agents, dendrimers are now being taken seriously as a candidate for a long-sought delivery agent for siRNA (gene silencing) therapy.

Tomalia named the molecules "dendrimers" and "dendritic polymers" based on the Greek word for tree.

He and the rest of the dendrimer community will have a chance to see that evolution's progress in 2007. In 2007 alone, dendrimers have attracted about a million dollars in DARPA funds for research into a device that would automatically keep wounded soldiers free from pain on the battlefield;

COURTESY OF STEVE KEINATH, MICHIGAN MOLECULAR INSTITUTE





Polyamidoamine (PAMAM), dendrimers taking about a month's worth of time for grow up to 7th generation

"I think dendrimer science has begun the serious evolution from academic to commercial,"

D.A.Tomalia

But there are still many barriers to widespread commercialization, the main one being the high cost and length of time it takes to produce them.

There is only a handful of applications and discoveries that are currently considered commercially viable and worth pursuing due to the very high cost of producing even small quantities of dendritic molecules.

For example, the cost of making the more commonly used ploy(amidoamine), or PAMAM, dendrimers can several hundreds of dollars per gram while also taking about a month's worth of time. Producing just 300 milligrams of a 7th generation polyamidoamine, or PAMAM, dendrimer costs approximately \$600.

On the other hand, the production time of Priostar, is expected to be three steps over five days for about \$10 a gram. This decrease in cost and time are due to the cleaner, faster chemistry, less reagent waste, lower levels of dilution.

Priostar Commercialization

To be continued

