

August 2003

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AIDS RESEARCH

# The amfAR Treatment Insider

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## Big Leaks in the Bristol Pipeline

by Kristen Kresge

Analysts were startled when Bristol-Myers Squibb (BMS) announced two years ago that it was acquiring DuPont Pharmaceuticals for \$7.8 billion. Rumors circulated among investors that the purchase price was nearly \$2 billion more than the next highest bid. It was not clear how Bristol expected to recoup this large an investment. That question looms even larger now: Bristol has abandoned DuPont's entire stable of promising new HIV drugs one after the other. The takeover's net result so far has been to increase Bristol's marketing prowess by enlarging the range of "once-daily" HIV drugs Bristol offers while killing off the potential new competition represented by DuPont's experimental agents.

### Falling by the Wayside

DuPont was a minor player in the pharmaceutical world that established itself through the rapid development and marketing of its HIV drug efavirenz (Sustiva). The aggressive work of DuPont's small research team was something BMS needed to energize its struggling laboratories, and Bristol early on proclaimed its interest in adding the DuPont scientists to its organization.

DuPont brought with it a particularly rich pipeline of experimental HIV drugs. The company had an active clinical program developing all three standard HIV drug classes: protease inhibitors, nucleoside analogs and non-nucleoside reverse transcriptase inhibitors (NNRTIs). Some of these "second generation" compounds had already entered clinical trials and held promise for treating drug-resistant virus.

But Bristol already had its own HIV drugs to promote. The nucleoside analogs d4T (Zerit) and ddI (Videx) were consistent big sellers and are available in new once-a-day forms. There is also a once-daily protease inhibitor, atazanavir, for which Food and Drug Administration (FDA) approval is now imminent (see accompanying article). By adding once-daily efavirenz to this trio, Bristol obtained a complete range of HIV drugs for combination therapy and could immediately challenge GlaxoSmithKline for dominance in the HIV market.

How BMS would take advantage of DuPont's candidate HIV drugs was a subject of speculation. In the best of times, Bristol's record of drug development has

been less than stellar — it took the company seven years to bring atazanavir to market after purchasing it from Ciba-Geigy (now part of Novartis). Observers feared that the new DuPont drugs would also get bogged down, or even suppressed altogether, by the pressure to show immediate income from the DuPont acquisition as well as by marketing considerations. Although the new drugs may not be groundbreaking new options, delaying them could be a huge loss to the growing number of people with multidrug-resistant HIV.

Bristol officials at first maintained that the DuPont second generation NNRTI, DPC 083, could come to the market in 2003, helping those for whom efavirenz and other NNRTIs no longer work. But DPC 083 is nowhere to be seen, and DuPont's other experimental agents have also quietly fallen by the wayside.

The effort to expand Bristol's research team also quickly faded. Layoffs at DuPont began shortly after the acquisition in departments outside of research and development, but no department was spared. Last November, Bristol announced it was closing all of the former DuPont sites in Delaware and dismissed most researchers at these sites.

"The only thing they took from DuPont was Sustiva," said Dr. Michael Otto, Chief Scientific Officer of Pharmasset, a small research company in Georgia. "They kept virtually none of the people." Otto worked in the virology program at DuPont for ten years and knew many of its members.

### The First to Fall

The first promising drug abandoned by BMS was DPC 817, a potent nucleoside analog that was in phase I trials. This compound was licensed by DuPont, along with a family of other compounds from Pharmasset, an Atlanta biotech founded by noted HIV drug creator Raymond Schinazi of Emory University.

After buying DuPont Pharmaceuticals, several Bristol executives gathered at DuPont's Wilmington, Delaware site to hear presentations by members of the virology team on the status of their pipeline. The DuPont staff was told not to bother with DPC 817. Bristol already had two nucleoside analogs, and it was not looking for others. "It was announced that they weren't interested," said one DuPont virologist present at the gathering.

Shortly after deciding on the acquisition in the spring of 2001, Bristol decided to return DPC 817 to

Pharmasset. Yet at a community meeting in February 2002, officials from BMS reported that DPC 817 was dropped due to animal toxicity.

"That is a lie," said Otto. In fact, after the drug's return to Pharmasset, Otto and his company continued with development and restarted human trials of their own. Otto does acknowledge that the drug is not tolerated in rats, but he says that no obvious safety issues have yet arisen in humans.

BMS now seems to agree with Otto. In a recent interview, Brian Henry, the Associate Director of Virology in Corporate Affairs at Bristol, said the reason for returning DPC 817 to Pharmasset was a business decision based on a "very robust" BMS portfolio. Henry would not comment on any previous reports of the drug's toxicity.

Single doses of DPC 817 in treatment-naive volunteers resulted in a mean 0.44 log (64%) drop in HIV viral load. Pharmasset says it is developing this drug (now dubbed "Reverset") primarily for salvage therapy based on its in vitro effect on HIV with drug-resistance mutations.

### Prioritizing its own Protease Inhibitor

Bristol also quickly stalled DuPont's early-stage protease inhibitor program. Before the sale to BMS, two second-generation protease inhibitors (DPC 681 and 684) completed phase I trials. Although these compounds were not pursued, their progress spurred a further attempt to find protease inhibitors similarly active against HIV with resistance to current protease inhibitors.

In the introductory talks between DuPont virologists and BMS executives, little time was reserved to discuss the status of the five-year, 50-person protease inhibitor program. Five minutes, to be exact. "The impression was that they had a PI [atazanavir] so that was of less interest to them," said the DuPont virologist present at the meeting.

Bristol has remained focused on atazanavir and has, for now, overlooked DuPont's candidate protease inhibitors. No official statement could be obtained as to their current status.

### The Bigger They Are, the Harder They Fall

The most difficult and complicated story of the DuPont pipeline is DPC 083. This drug was chosen as the lead compound to back up efavirenz. Resistance mutations that severely limited the potency of

efavirenz were less likely to impact 083. Activity against resistant virus made it a promising new compound and hopes were high for its success at Bristol.

Prior to the DuPont sale, two phase II trials with 083 were in progress (DPC083-201 and -203). The 203 study faced a multitude of complications. Many sites were unable to enroll the required number of participants due to the strict entry criteria. To accelerate enrollment, DuPont officials began changing the study protocol while the trial was in progress. The maximum allowable viral load at entry was raised from 5,000 to 10,000 copies/mL — a more common viral load cutoff — halfway through the study.

But enrollment in the study lagged even after raising this limit. Controversies surrounding prior drug experience and eligibility for the trial arose on a regular basis. Study coordinators were on the phone with DuPont officials daily trying to enroll seven or eight volunteers.

The planned study size was 150, equally divided between the 100- and 200-mg doses. The 200-mg dose was evaluated only in Europe because the US FDA had safety concerns about this dose. The total number of volunteers ended up at 31. With so few participants, it became difficult to extract any useful data.

“This was the most poorly written protocol that I have run. Things started popping up after the fact, and we were losing touch with hard science,” said a staff member at one study site.

Yet none of these problems surfaced until after Bristol took over. The staff member speculated that the quality of the 203 study was affected by staffing changes that occurred at DuPont as the official sale date approached.

In study 203, 45% of the volunteers (14 of 31) were expelled because of protocol violations. The problem was these volunteers had prior protease inhibitor therapy, which, according to Bristol, made them ineligible. There is still some confusion here. The trial site staffer insists that official protocol only excluded people who dropped their protease inhibitor because of HIV breakthrough.

But Bristol remained publicly committed to 083. It did appear overall, from this and other studies, that 083 was a potent drug with a safety profile similar to efavirenz. Rash appeared to be worse but the efavirenz-associated effects on the central nervous system seemed less prevalent.

Even if this phase II study was completely bungled, it need not be the end of DPC 083. In an oral presentation at the 2002 Conference on Retroviruses and Opportunistic Infections, Bristol (and ex-DuPont) researcher Nancy Ruiz stated in her conclusion that a new phase II trial was “in planning.”

Then development of 083 was halted without public announcement. “Currently we have stopped development of DPC 083. We are not moving forward,” Henry confirmed this spring. He said that Bristol dropped 083 simply “because efficacy in NNRTI failures was not established.”

Ruiz had told some clinicians working on the 203 study that another of the four NNRTI candidates would be explored, but at least one of these doctors deems it unlikely. BMS would not confirm any work on other NNRTIs.

### Don't Get Your Hopes Up

“BMS had a different niche. We were geared towards second generation compounds,” commented Susan Erickson-Viitanen, former Executive Director of Virology at DuPont Pharmaceuticals. “We thought Sustiva is a good drug — what will we do next?” Viitanen sees Bristol focusing more on new drug classes in the future. “Their entry inhibitor is a totally new thing,” she noted.

Bristol's new entry inhibitor has an unproven mechanism of action and remains in very early development. Although Bristol representatives have stated that commitment to their HIV program remains strong, the company may have squandered DuPont's more advanced improvements on conventional HIV drugs. Bristol is now mired in financial scandals, involving exaggerated profits, and its stock price has plummeted. Its financial decline threatens any hope that the DuPont compounds will see the light of day. Now, more than ever, Bristol is inclined to protect the profits from its established drugs.

In the aftermath of Bristol's weakened position, rumors of the company's sale to GlaxoSmithKline surfaced this spring. The rumors were based on the apparent “fit” between BMS and GSK products. But Bristol's handling of the DuPont acquisition, and its adverse consequences for those with HIV, is a warning against concentrating research and marketing muscle in one giant corporation.

## Atazanavir's Debut

by Kristen Kresge

The second anti-HIV drug to hit the market in 2003 will be Bristol-Myers Squibb's protease inhibitor atazanavir (Reyataz). It may not be as groundbreaking as the introduction of this year's first drug, T-20 (Fuzeon). Still, atazanavir will continue the trend toward simplified HIV regimens due to its once-daily dosing.

### Where's the Advantage?

Atazanavir does not stand out from the other protease inhibitors in terms of efficacy. BMS conducted several phase II and III studies to establish the efficacy of atazanavir in relative to such approved drugs as nelfinavir, efavirenz and Kaletra. In persons without prior treatment, atazanavir's efficacy appeared similar to nelfinavir, the most popular protease inhibitor.

More surprising were the results of the trial comparing atazanavir with efavirenz, Bristol's potent once-daily non-nucleoside reverse transcriptase inhibitor (NNRTI). That study enrolled 805 treatment-naive volunteers who received Combivir (AZT and 3TC) along with either atazanavir or efavirenz.

After 48 weeks, 37% of volunteers receiving efavirenz and 32% receiving atazanavir had undetectable viral loads (less than 50 copies/mL). CD4 cell increases and adverse event rates were similar in both groups. Although efavirenz looked slightly better than atazanavir, its success in this trial was unexpectedly low compared with previous studies.

One advantage is atazanavir's evident lack of effect on blood lipids. People on anti-HIV combinations usually experience increases in cholesterol and triglyceride levels, which may put them at risk for cardiovascular disease. Atazanavir thus promises to reduce one of the major long-term side effects of continued HIV treatment.

Another potential advantage is atazanavir's resistance profile. HIV that develops resistance to atazanavir commonly has a mutation not seen after exposure to other protease inhibitors.

### Atazanavir in Salvage Therapy

But atazanavir has not shown well in treatment-experienced patients with resistance to the available protease inhibitors. One phase III trial compared atazanavir with Kaletra (a protease inhibitor combination of

lopinavir plus ritonavir). This study enrolled 229 volunteers with an average of three years prior HIV therapy. Everyone had failed a drug regimen that included at least one protease inhibitor. The volunteers were randomized to receive either atazanavir or Kaletra in addition to two nucleoside analogs selected for maximum effect in each person.

An interim analysis at 24 weeks found that atazanavir was less effective than Kaletra. In the Kaletra arm, 52% of study participants achieved viral loads below 50 copies/mL whereas only 41% did so in the atazanavir arm. Atazanavir's activity was significantly diminished in study volunteers with previous exposure to two protease inhibitors. Overall, the percentage with viral loads below 400 copies/mL was 80% in the Kaletra group and 60% in the atazanavir group. In those with two or more prior protease inhibitors, the respective percentages were 85% for Kaletra and 39% for atazanavir.

Hopes for atazanavir in that population are pinned to a new study of ritonavir-enhanced atazanavir compared to Kaletra in persons who have failed two or more HIV regimens. Atazanavir was given at a reduced 300-mg dose (the standard amount is 400 mg) along with ritonavir, which greatly slows atazanavir's breakdown in the body. Bristol could not explore using a higher dose of atazanavir because of the drug's tendency to cause high bilirubin levels in the blood. High bilirubin results from a block on the liver's ability to eliminate excess iron. It can lead to jaundice. Adding ritonavir, then, is the only strategy at hand to make the drug more effective against resistant HIV.

Adding the ritonavir lessens the simplicity of atazanavir's dosing. Ritonavir also is a strong booster of blood lipids and is toxic to the liver. These factors could obviate atazanavir's lipid-stabilizing effect, too, while complicating the jaundice that atazanavir can induce.

At the last minute, Bristol included the 24-week preliminary results of the atazanavir/ritonavir trial as part of its FDA filing. The overall atazanavir results were similar to Kaletra's — 39% in the atazanavir/ritonavir arm and 42% in the Kaletra arm achieved viral loads below 50 copies/mL. Kaletra seemed superior only in those whose HIV had four or more mutations conferring resistance to protease inhibitors.

## HIV Erupts in Russia

by Anne-christine d'Adesky

Off a highway leading from St. Petersburg stand several massive unadorned low-income apartment complexes, modern-day castles towering in the wind off the Baltic Sea. There are few residents to be seen in this barren landscape, but several people huddle outside an RV parked on a side road. They smoke and chat before stepping back inside.

The RV is a mobile clinic that belongs to Humanitarian Action, a new nonprofit organization affiliated with the French humanitarian agency Médecins du Monde (Doctors of the World), an offshoot of the better-known Médecins sans Frontières (MSF; Doctors Without Borders).

It parks here every afternoon, at one of two mobile needle exchange sites that are viewed as the frontlines of Russia's battle against AIDS. A short time after its arrival, people quietly begin slipping out of the surrounding buildings and make their way over. Inside, space is so cramped that counselors and nurses must shuffle their legs to allow others to come and go. Most stop at a small window where, after giving their first names only, they hand over used syringes in exchange for fresh ones. Over 230,000 syringes are given out a year by the program, and 98% are traded for used ones.

The program is one of 43 harm reduction programs in the 12-member Commonwealth of Independent States (CIS), backed mostly by money from the US-based Soros Foundation and its Open Society Institute. The AIDS Foundation East-West (AFEW), an umbrella advocacy network that grew out of MSF-Holland's projects in the CIS region, sponsors their work.

Inside the trailer, new clients step further back for an intake checkup by a nurse or doctor. Then they receive counseling and testing for HIV, tuberculosis (TB) and hepatitis. Many clients have all three. They leave with referrals for follow-up tests and care at the city's AIDS program or the specialty AIDS ward at Botkin hospital. Some are referred to TB hospitals for X-rays and treatment or to STD clinics for gynecological and obstetrical services. More and younger clients are getting pregnant, and few have access to prenatal care. Short of being a full-service medical provider, the program provides a bridge between groups at high risk for HIV and Russia's sprawling public health system.

"We are a syringe-exchange point, but we noticed the need for care and treatment is very great in this popula-

tion," explained Alexander Tsekhanovitch, who heads the mobile program. "We feel that our program is not a polyclinic or an ambulance-on-wheels. It is a step between real life or the street and the health services of the city. We try to organize a way, a route, and we try to connect them with real people. We bring them in touch — patients and doctors. Before we started here, there was no one connection between official services and these vulnerable groups. At the same time," he conceded, "what we are doing is very limited."

Many clients live on the street and need an array of services: food, jobs, housing. At the top of the list is drug addiction treatment, which is seriously lacking in Russia. Methadone use is outlawed and there are few rehab programs. Most clients shoot heroin; many are hardcore addicts. Like sex workers, they tend to avoid anything official, including city healthcare services, fearing arrest or discrimination. And for good reason, Tsekhanovitch reported. "The general attitude toward drug users is very negative. The basic policy has been to lock them up. It is the same with prostitutes. Now you are adding HIV into the mix. I hate to say this, but many people would be just as happy to see them all die."

### No Safety in Numbers

Harm reduction projects were just getting off the ground in 1999, a turning point in the epidemic, say health officials. Since that year, statistics show it has exploded at a rate that these officials call an E-curve, with annual new infections more than doubling the entire caseload of the previous period. Up until now, the bulk of those affected have been drug addicts and sex workers who typically turn to prostitution to support their own drug habit. The drug problem has fueled crime, and many have landed in prison, where HIV testing is mandatory.

Today, about 3% to 4% of the total prisoner population has HIV. Many are released with new infections of drug-resistant TB and hepatitis — crises that shadow the AIDS problem. Surveys have found that sex and drug use are common in prison while medical treatment is limited outside small pilot projects like those run by MSF-AFEW.

Over the past year, Russian government warnings have started to match doomsday forecasts by AIDS groups that describe the epidemic in catastrophic terms, a giant waking bear that no one can fully grasp, never mind contain. Russia officially claims 230,000 HIV cases and

800 AIDS cases, including 191 children. Six hundred people have died over the years. This spring, Vadim Pokrovsky, the country's top AIDS official and head of the federal Center for AIDS Prevention and Treatment in Moscow, put Russia's HIV caseload at 1.5 million, with four to eight hidden cases for every documented one. These numbers are based on some 2 million mandatory HIV tests carried out in the general population each year for the past decade.

"The surveillance system is not useful if you don't have controlled sites or control groups among the highest risk groups," said Pedro Chequer at the United Nations AIDS Programme (UNAIDS) Moscow office. He worries that low-ball estimates are missing the more serious situations. "They say they have 240,000 people but that AIDS cases are less than 1,000 — that's not possible," added Chequer, who helped set up the much-lauded national AIDS treatment program in his native Brazil. "Look at Brazil: it has 700,000 people with HIV and 230,000 AIDS cases. So," he shrugged, "something is not right there." But Pokrovsky maintains that the low AIDS caseload reflects HIV's late appearance in the region.

Compared with elsewhere, the epidemic in the former Soviet bloc has a very young face. Eighty percent of HIV infections are in people under 30, and 20% are teenagers. In the central Asian republics, half of all cases are in youth under 20. The epidemic was first concentrated in Moscow and St. Petersburg, but has spread to poorer, remote regions like Siberia, prompting one US political analyst to predict that the epidemic in Eurasia, if unchecked, could one day surpass that of sub-Saharan Africa's.

There are 500 to 800 newly registered HIV cases a week and a growing percentage are linked to heterosexual transmission, not drug use or homosexual contact. Federal statistics capture the trend: in 2001, the ratio of male-to-female cases was 10:1; now it is 4:1. At the mobile trailer site, the ratio has reached 1:1 among new cases. The average age of infected girls also has dropped to become 2.5 years younger than boys.

Behind these figures is a generation of Russian teenage girls who become heroin addicts, enter sex work, and then contract HIV and hepatitis. Throughout the region, a growing number of infants born to HIV-positive, drug-addicted women have been abandoned. These orphans live in hospitals because no orphanages in Russia will accept them.

HIV is also rising among street children. At age 9 or 10, they start sniffing glue; by 14 they are in informal gangs, shooting drugs, having sex with each other, pick-

ing up and passing on HIV. "We are talking about a situation that is unimaginable, even to us," admitted Tsekhanovitch. "We are still a little afraid to evaluate the status of things."

### A Dearth of Dollars and Rubles

Outside of the Health Ministry, critics say AIDS is still not a priority for many political leaders. President Vladimir Putin has yet to make a public speech about the threat. Until now, Russia has had no national AIDS treatment or prevention program, and regional programs and NGOs have led the charge. The ban on methadone and drug maintenance programs is another crisis of leadership. The Russian government has failed to invest a ruble in harm reduction programs, leaving foreign donors to support the few local support programs for drug addicts.

Right now, the federal AIDS budget is a paltry \$3.7 million dollars. The average anti-HIV combination therapy costs \$7,000 a year. "If you have 230,000 people, you see that raises a big problem," said Pokrovsky, who has become outspoken on the need to increase the federal budget. "About \$2 million is directed to treatment out of this, and this will be enough only for several hundred. In a year, I expect, there will be many more patients and not a lot more money." He estimates that \$65 million is needed to confront the epidemic.

Anti-HIV treatment is free in Russia to those who qualify but is strictly controlled. It is provided only through city or federal AIDS centers. In Moscow and St. Petersburg, a proof of city residency is required to obtain HIV drugs free of charge. By Pokrovsky's count, around 1,000 of 15,000 HIV-positive Muscovites were receiving triple-drug therapy from the Moscow AIDS center in April. About 50 more were on a waiting list for the drugs. In the CIS states as a whole, 10,000 people were on treatment last year, out of 80,000 identified HIV-positive individuals.

"In Moscow, it isn't such a problem to get the drugs," said Roman Dudnik of AFEW, "but it is a problem in other places. In the cities where the oil industry is richer and money is available, the AIDS centers are better set up and more treatment and testing is available. But in many regions, you can't do a CD4 or viral load test, so it's hard to know how many really need treatment."

"With respect to HIV drugs, it's a tragedy and an outrage," said Masha Gessen, a well-known journalist who works for a leading Russian online news service. "It's provided only to a few people and specifically to people who are registered to live in those cities and are not drug users. So that rules out 90% of the people who may potentially

benefit.” Gessen has a friend without residency papers who recently sought treatment from the Moscow city AIDS clinic and was threatened with deportation.

The reality is that many HIV-positive people are in prison serving drug sentences. There, HIV treatment is limited aside from pilot MSF prison programs. “I am afraid that thousands of youth who got HIV infection in the last three to five years will die very soon, in the next years,” said Gennady Roshupkin, one of Russia’s leading HIV-positive activists. “Because, for a lot of them, HIV specialists can’t do anything.”

Over the past year, the situation has improved, due to activist and NGO pressure and behind-the-scenes brokering by MSF, the Open Society, UNAIDS and the World Health Organization. A national AIDS advisory council is being formed that will include HIV-positive groups, and the first regional meeting of CIS AIDS activists was held in April in Minsk, with help from US activists. The meeting concentrated on the obstacles to treatment information and access.

Russia recently accepted two World Bank loans, \$50 million for HIV/AIDS programs and \$100 million to fight TB. The money will go to mass media campaigns, among other priorities. Russian health officials are now drafting a national plan and a grant proposal to the Global Fund to Fight AIDS, Tuberculosis and Malaria. At the moment, there are two competing proposals: one by public health officials and another by an elite academic group led by Pokrovsky’s father, who heads the country’s medical academy.

### Unlocking the Doors to Treatment

The cost of treatment remains a big hurdle. The state produces two drugs: AZT and a homegrown AZT derivative. It has registered 12 brand-name medications, and Trizivir will soon be added to the list. With the potential Global Fund money, Russia could opt for cheaper generics, but activists worry that it will avoid this alternative. “Russia is hoping to become a member of the World Trade Organization and doesn’t want to be seen as taking a position against patents,” said Gessen. Off the record, one top health official said that Russia would prefer to negotiate a steep discount on patented drugs from companies with whom it has established relationships. “This is a political question,” he admitted. At UNAIDS, Chequer is pushing Russia to revive its moribund pharmaceutical industry and produce its own generics, just like Brazil.

Another hurdle is the dilapidated state of the public health system. Activists say it retains vestiges of the old

heavy-handed Soviet bureaucracy. HIV testing is mandatory for prisoners, pregnant women, blood donors, soldiers and those needing surgery, but in practice, it is routinely done on those seeking care from health clinics, often without their knowledge or consent. On paper, government AIDS programs include voluntary counseling and testing services but, Gessen said, “There is really no such thing as consent, regardless of what the government may say. There is no protection of the rights of people with HIV, who, for the most part, happen to be drug addicts and prostitutes — forget it.”

Many citizens have obligatory medical insurance and in theory, are freely treated at public hospitals and polyclinics that house a variety of specialists under one roof. Infectious diseases like TB are treated in separate clinics, as are STDs. Since HIV-positive drug users may be coinfecting with STDs, TB and hepatitis, treatment is not well coordinated. Those released from prison or rehab programs are often lost to follow-up due to a lack of adequate discharge planning.

Compared with the city hospitals, which are rated as mediocre to terrible by Russians, the AIDS clinic at St. Petersburg’s Botkin hospital receives good marks. Botkin is a huge state facility that treats 38,000 inpatients a year and 70,000 on an outpatient basis. The AIDS unit offers counseling and testing services, clinical care, surgical services and treatment to qualified patients. A special obstetrical unit exists for pregnant women, and AZT and rapid testing are offered to prevent maternal HIV transmission. Under treatment guidelines drafted by Pokrovsky, HIV treatment is available to anyone with a CD4 count under 300 cells/mm<sup>3</sup>, a viral load above 60,000 copies/mL or HIV-related symptoms. AZT, 3TC and indinavir constitute the standard first-line therapy.

Around 120 people began triple-drug treatment at Botkin four years ago, and the results have been very positive so far. There have been no deaths in the group, and serious AIDS cases have generally recovered. “Our experience is quite positive,” said Dr. Vladimir Musatov, head of the Botkin AIDS ward. But medicine, tests and materials are limited at the hospital, and patients sometimes pay for services. Although viral load tests are available, there is an emphasis on clinical monitoring and on less costly CD4 cell tests.

Dr. Musatov acknowledged that even with drugs, management of coinfecting TB/HIV patients is an enormous challenge, and almost impossible in active drug users. Outside Botkin, things are worse. “The conditions in the polyclinics are really quite low. There is poor train-

ing, equipment, especially laboratory equipment,” Dr. Musatov confirmed. “The really successful treatment of patients in my mind is in specialized hospitals.”

The nearby Republican Hospital offers care to non-residents, with three departments specializing in care for children with HIV. Some belong to an initial group of 270 infants who contracted HIV in pediatric hospitals in 1989 from contaminated blood and equipment; an official scandal branded the Elista incident. Half the children are now dead; the other half began getting AZT in 1991, then dual and now triple therapy. One hundred of the 130 survivors receive treatment. As a group, they constitute Russia’s long-term survivors. Some spent most of their lives growing up in hospitals.

“When we start to treat our children, they are very small, but they grow very quickly,” said Dr. Yevgeny Voronin, a strong advocate for HIV-positive children. But adherence is a major problem for children and their caregivers, he noted. “When a child is psychologically exhausted, they prefer a miracle: one pill — and health. It’s very difficult.” The drugs are not working as well in some of the long-term survivors who have had HIV for 13 years and received mono- and dual therapy. Some have developed drug resistance. Side effects such as metabolic problems and lipodystrophy have also surfaced.

In 1997, many AIDS centers began providing short-course AZT to pregnant mothers to prevent mother-to-child transmission (MTCT). Mothers who fail to get prenatal care are supposed to receive rapid testing during delivery. But only a few sites have rapid tests, and drugs are missing in many hospitals. In a controversial move, Dr. Pokrovsky says the government now plans to automatically provide MTCT drugs to all pregnant women who are intravenous drug users, eliminating the need for consent or testing.

## Love Is the Drug

To AIDS groups, widespread ignorance and stigma surrounding the disease still facilitate the isolation of people with HIV. The vulnerability and instability of drug users, sex workers and street children make these groups especially hard to mobilize.

Sergei, 25, is a volunteer coordinator of a mixed support group that meets at Botkin hospital and is open to HIV-positive and -negative people. It is one of around ten support groups in the entire country. Sergei was serving his military duty in the north when he tested positive for HIV during routine screening for new recruits. He openly admitted to doctors that he had used drugs, and was immediately isolated in a diagnostic ward for 25 days with five other soldiers. “If you have this diagnosis, people are afraid of you as if you had the plague, or are a leper,” he said. His group was fed separately and only briefly allowed outside the isolation ward to smoke and talk to people. “People would pass by and peep into this window like we were animals in the zoo,” he recalled bitterly. At 5 AM one day he was woken, taken to the train station, and sent packing without food or money.

“Like everyone, I was afraid and I was totally isolated,” said Sergei. “People are just told they are going to die, and there is so much misinformation. For me, being with those other guys who had HIV helped. We supported each other. That’s why I believe we have such an important role to play now.” He said a close friend who was recently diagnosed with HIV just committed suicide. Another friend was on the verge of killing himself when Sergei met him. “These people feel desperate, like they are the only ones,” he recalled. “Nobody is helping them.”

“The first wish of every person is to get that magic pill. But from my point of view, in Russia now, we have more need for psychological support, for jobs, for AIDS prevention — even before treatment,” said Roshupkin. “The doctors and medical professionals concentrate on access to pills. But they have no skills or knowledge about how to work with a person who has to take a pill every day. Support is more important. It can’t be forgotten. That’s why support groups are so important. All of this is just beginning in Russia. It is the beginning of a movement, but we have so much work to do. As activists, we need to show all these young people how to live and stay healthy, not just survive, but how to carry on with their lives.”

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