XY Inc. and Audubon Nature Institute of New Orleans Achieve Another Scientific Breakthrough: The World’s First Sex-Selected Cats

With the birth of the world’s first sex-selected kittens, a common house tabby has become queen of the jungle, at least in the feline kingdom, which includes 36 exotic species — almost all of them endangered.

For the first time ever, domestic kittens were born with their sex predetermined using XY® Sex Selection Technologies, a cutting-edge sperm-sorting technology developed by XY Inc.

A litter of healthy, hungry kittens, produced from embryos created with sexed sperm, was born at Audubon Center for Research of Endangered Species (ACRES) in New Orleans on Oct. 11.

The births advance the science of high-tech assisted reproduction by confirming that fresh cat sperm can be successfully shipped to a sorting facility, processed, return shipped and remain viable to produce healthy sex-selected felines. The success is the result of a research collaboration between ACRES and XY Inc., in which XY Inc. developed the technology specific to cat sperm, and ACRES adapted existing protocols to work with sorted sperm.

“By developing new reproductive technologies and reintroduction techniques necessary, we are working to ensure the long-term survival of endangered species,” said Audubon Nature Institute Senior Vice President and ACRES Director of Research Betsy Dresser.

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Take a Bow

LETTER FROM THE XY INC. CHIEF EXECUTIVE AND PRESIDENT

When XY Inc. was formed May 28, 1996, our founding collaborators Colorado State University Research Foundation, Cytomation and USDA agreed this little company held promise.

What has become abundantly evident over the last decade to the world of animal husbandry is this: XY Inc. has matured into the undisputed global leader in the sex selection of animals.

The enormity of this accomplishment is the product of vision and commitment by many. XY Inc. would not be here today without the steady, solid scientific advancement by XY Inc. scientists and global research collaborators; the sustained belief and backing by its faithful stockholders and the commercial adoption by XY Inc. licensees. To all, I, on behalf of XY Inc., say, "Thank you and congratulations!"

- We can trace the soundness of our scientific achievements to top global scientists in sperm metabolism; viability; freezing; and early sperm sorting in rabbits, pigs, cattle, sheep and horses. These world researchers aligned their years of academic study to create the highly orchestrated process of refining sex-selection techniques in animals. Hats off to Dr. Larry Johnson; Dr. George Seidel; Dr. Duane Garner; Dr. Chris Polge; Dr. David Cran; Dr. Chris Maxwell; Dr. Detlef Rath; Dr. Roger Gerrits; and XY Inc’s first and current lab manager, Research Physiologist John Schenk.

- Over its first 10 years, XY Inc. has developed and now owns more than 350 patents that are critical to XY® Sex Selection Technology, the only proven, commercially viable sex-selection technology in the global market.

- We have been instrumental in research and application that have resulted in the first ever sex-selected animals in such wide-ranging species as the horse, sheep, pig, elk, bison, dolphin and, most recently, the cat. These efforts, whether on behalf of agriculture or conservation efforts, have brought XY® Sex Selection Technology to the forefront of scientific and commercial circles.

- Our reach beyond our “hometown” has extended us into the “global village” where today we have research collaborators and commercial licensees in almost every continent—North America, South America, Europe, Asia and Australia.

- And, we can take special pride in the fact that we are fully solvent, and we continue to grow our resources through innovative licensing agreements, propriety and successful reagent products and an expanding tool box of technical parts and service offered to licensees.

It has not been an easy trip from our beginning days to where we stand today. I’m sure you know well we have weathered the obstacles of early skepticism; challenges by a passing parade of hopeful competitors; and even court challenges to XY Inc.’s right to seek fair and proper business dealings.

Today, we are past most of these obstacles. We have never hesitated in our efforts to continue to improve the rarified “art” of sex selection in animals, to serve animal welfare and maintain a steady course in the face of major odds.

We appreciate your confidence in XY Inc. We look forward to our next decade with curiosity, courage and vigor.

Dr. Mervyn Jacobson
President and Chief Executive, XY Inc.
Colorado State University Research Foundation and XY Inc. Sign Historic Agreement

The decade-long, fruitful relationship between XY Inc. and Colorado State University Research Foundation, one of XY Inc.’s founders, came full circle recently. On Sept. 29, CSURF assigned to XY Inc. more than 140 patents jointly developed by Colorado State University and XY Inc. over the last 10 years.

Said CSURF CEO Kathleen Henry, "XY Inc. is now 10 years old and has grown up, and it’s time for XY to graduate as a fully matured commercial enterprise. This exchange of patents is good for XY, for CSURF and for CSU."

In addition, XY Inc. bought back 1.1 million XY Inc. shares formerly issued to CSURF.

The milestone event in the relationship of XY Inc. and CSURF got its start in December 1996 when CSURF and XY Inc. signed formal documents that authorized CSURF to assign all rights and obligations under its license agreement with the USDA (re: Johnson Patent) to XY Inc.

In addition, in those early years XY Inc. gained intellectual property rights, "the crown jewels" in the race to commercialize, from another XY Inc. founder, Cytomation, and rights and intellectual property from several leading research institutes globally.

And, the persistent, scholarly efforts of the original XY Inc. research team cannot be overlooked. In June 2000, the US Patent Office issued the first XY Inc. patent, "System for Improving Yield of Sexed Embryos in Mammals." The inventors listed on the patent are Colorado State University’s venerable George Seidel, a “father” of sex selection; and John Schenk, XY Inc.'s key reproductive scientist today. Lisa Herrickoff, an early, former employee, also is listed as a member of that significant research team.

"All of these early patent achievements and those we continue to gather today mark an incredible passage by XY Inc.,” said Jacobson. “For a little company, we have garnered a mighty presence in the research and commercial world of sex-selection in non-human mammals."

Colorado State University Professor George Seidel, a world-renown researcher in the field of animal reproductive physiology, was XY Inc.'s first Director of Science.

“The signing of these documents is such a simple act, yet, it reflects 10 years of intense commitment, creativity and success by literally hundreds of people who are all part of the process to take cutting-edge technology from the laboratory to the market.”

- Dr. Meryn Jacobson
CEO XY, Inc.
Happy 1st Birthday to the World’s First Sex-Selected Dolphin

Happy 1st Birthday to SOFI, the world’s first sex-selected marine mammal. The Atlantic bottlenose dolphin was born October 2005 at SeaWorld San Diego, using XY® Sex Selection Technology.

“SeaWorld’s sex-selected dolphin calf is a first for the zoological community, which works to provide optimal social environments while managing genetically diverse populations,” said Dr. Justine O’Brien, reproductive physiologist. O’Brien is a University of Sydney Research Fellow from Australia and an XY Inc. research collaborator. She specializes in wildlife species sperm-sexing research.

“There are many species, such as dolphins and elephants, which in the wild exist in single-sex dominated groups. The ability to preferentially produce females or males will allow zoos to better manage these species.”

In October 2004, O’Brien and Dr. Todd Robeck, corporate director of theriogenology at SeaWorld San Antonio, artificially inseminated Sandy, a 26-year-old Atlantic bottlenose dolphin at SeaWorld San Diego (www.seaworld.org) with sorted sperm. High accuracy of the procedure was demonstrated in trials during 2003 and 2004 with sexed-sperm samples containing greater than 90 percent of the desired sex.

On Oct. 6, 2005, Sandy gave birth to a healthy female calf under the watchful eyes of SeaWorld’s dolphin trainers and veterinarians.

The successful birth was a collaborative effort among SeaWorld’s veterinary, animal care and training staffs; XY Inc. and others.

While this reproductive technology will significantly assist zoological institutions around the globe to optimally manage species’ genetic diversity, the knowledge gained from this scientific research may ultimately have application in marine and terrestrial animals in the wild, including endangered species.

“Our technology was instrumental in this successful application of sperm-sexing technology to bring about this first sex-selected female dolphin.”

Mervyn Jacobson
XY Inc. CEO

The world’s first sex-determined dolphin at SeaWorld San Diego.
XY Inc. Researchers Among Select Few to Have Poster Chosen for Major North American Embryo Transfer Meeting

XY Inc. scientists John Schenk and Dr. Elizabeth Crichton were among a select group of international researchers to have their research poster chosen for presentation at the joint annual meeting of the American and Canadian Embryo Transfer Associations.

Schenk and Crichton, assisted by XY Inc. technician Steve Huffman, authored a poster based on their research pertaining to the use of sexed sperm with lactating Holstein cows.

In January 2006, Schenk and Crichton presented their results at the annual meeting of the prestigious International Embryo Transfer Society. Of the nearly 400 posters selected for display at IETS, the XY Inc. poster was one of only a few to be chosen for the North American joint conference, held in October in Ottawa, Ontario, Canada.

The recommended use of sexed sperm until now has been limited to heifers. The XY Inc. poster reported the results of a field trial conducted with 172 lactating Holstein cows approaching 80 days in milk (DIM) to determine pregnancy rates, following artificial insemination with cryopreserved sorted sperm. The study compared doses of 2 million and 10 million frozen, thawed sexed sperm with a conventional AI dose of 10 million unsexed, frozen, thawed sperm.

The study showed the pregnancy rate in lactating cows inseminated with sexed sperm was not significantly lower than that of unsexed sperm. However, the researchers cautioned the numbers of cows used in their study were limited, and the findings applied only to normal cycling cows that have reached approximately 80 DIM.

“XY Inc. continues to advocate the use of sexed sperm be limited to heifers,” Schenk said. “Meanwhile, large-scale lactating-cow field trials with sexed sperm are continuing.”

The XY Inc. lab team, headed by Reproductive Physiologist John Schenk (not pictured) conducts research, provides training and offers technical assistance throughout the year to licensees at their labs or at XY Inc.’s Fort Collins laboratory.

Top from left: Kathy Mean, laboratory support specialist; Steve Huffman, lab technician; and Dr. Elizabeth Crichton, research physiologist. Front from left: Lisa Massoudi, lab technician; Mindy Meyers, graduate student in equine science.
1. The MoFlo SX™ is designed specifically to sort sperm and is one of the most advanced flow cytometers in the world. It was designed and continues to be manufactured by DAKO-Cytomation exclusively for XY Inc. and its worldwide licensees and research collaborators.

2. XY Inc. achieves the first pregnancy in the world of a mare using sorted sperm and low-dose surgical insemination. “Call Me Madam,” the first horse in the world whose sex was selected prior to conception, was born Aug. 6, 1998.

3. XY Inc. researchers achieve pregnancies in heifers, using low-dose, sorted, frozen and thawed sperm. The resulting calves were born in early 1999, paving the way for worldwide commercialization of this technique.

4. Charity, Clover and Cloe are the UK’s first-ever female calves whose sex was determined before conception using artificial insemination and XY® Sex Selection Technologies.

5. The world’s first foals are born from mares impregnated via artificial insemination combined with low-dose sexed semen.

6. Cogent, a British membership-based breeding program and XY Inc.’s first licensee, announces its entry into the market with Sexed Advantage, sorted cattle sperm.

7. The Livestock Industry Association of Japan (LIAJ) signs a research collaboration with XY Inc.

8. Britain’s Ministry of Agriculture, Fishery and Food awards Cogent and XY Inc. first prize in the Science into Practice Award Program during a special ceremony at the House of Lords, London.

9. In January, to accommodate its expanding equine-breeding program, XY Inc. moves its headquarters and horse facilities to historic Moondrift, located in Fort Collins, Colo.

10. XY Inc. and Sydney University announce the world’s first sex-selected lambs conceived using low doses of sperm that were sorted, frozen, thawed and artificially inseminated into ewes.

11. The German Government Research Institute (FAL) produces the first piglets, using ICSI (intracytoplasmic sperm injection) and XY® Sex Selection Technology.

12. XY Inc. works with Australian researchers to combine sex-sorted equine sperm with embryo transfer to successfully produce Ballerina, whose dam is a high-quality polo mare.

13. CEO Mervyn Jacobson meets US President George Bush at a VIP reception hosted by Colorado Gov. Bill Owens. President Bush comments to Dr. Jacobson, “Doctor, you are the leading edge.”
14. First Lady is born, the world’s first foal produced from Call Me Madam, the world’s first sex-selected filly in 1998, and Augustus Primus (14B), the world’s first sex-selected colt in 1999.

15. XY-Mexico launches in July. Licensed to work with Mexican dairy and cattle farmers, XY-Mexico, CA d’CV, Torreon, Mexico, begins commercial sales of sexed straws of bull sperm.

16. Coyuete S.A, an early XY Inc. licensee and a leading cattle-breeding company in Argentina, also begins commercial sales of sorted cattle sperm in Brazil.

17. In November, the XY Inc. laboratory moves into new facilities on Research Boulevard in Fort Collins, Colo. The spacious 3,000 sq.-ft. space houses XY Inc.’s research team, sperm-sorting and processing laboratories.

18. In March, XY Inc. and Trans Ova Genetics, the global leader in embryo production and transfer, sign an agreement that allows Trans Ova, located in Sioux Center, Iowa, USA, to provide its customers with sexed cattle embryos.

19. In April, Inguran, XY Inc.’s first commercial U.S. licensee, begins to offer complete sexed-sperm services in conjunction with bulls custom collected at Genetic Resource International. Inguran is located in Navasota, Texas.

20. In August, XY Inc. and DakoCytomation jointly sign an agreement worth more than $10 million to work with GoldCattle Bio, Inc. and China National Animal Breeding StockExport/Import Corporation (CABS).

21. Dr. Mervyn Jacobson is named the Chief Technology Officer of the CABS Scientific Advisory Board.

22. In November, IND Lifetech (22B), which holds a pre-commercial license to produce cattle embryos for shipment to China, reports the birth of its first calves in China.

23. In February, XY-Mexico works with major Mexican dairymen to produce Mexico’s first sexed calves via XY® Sex Selection Technology.

24. In March, XY Inc. and L’Alliance Boviteq announce the signing of a commercial license agreement to apply XY® Sex Selection Technology to the Canadian cattle industry.

– In October, the world’s first sex-selected marine mammal, an Atlantic bottlenose dolphin, is born at SeaWorld San Diego. (story on page 3.)

– In September, CSURF and XY Inc. sign historic document. (story on page 4.)

– For the first time ever, domestic kittens are born with their sex predetermined. (story on page 1.)
XY Inc.’s Moondrift Headquarters Staff Takes Care of Business

Most of the daily behind-the-scenes administrative work of XY Inc. is handled by a small and energetic staff. As corporate needs have grown, XY Inc. has centralized many of its administrative functions under one roof. And, for those of you who have visited Moondrift, our headquarters, you know that actually means a suite of offices on top of a barn.

Housed on the picturesque 50-acre Moondrift grounds, once home to a top Morgan horse breeding and equestrian center, headquarters offices are situated in a unique structure built with a residence on top of the main horse stable.

While other stables may have mice in the rafters, XY Inc.’s has the hum of a busy office. Thom Gilligan, general manager, handles a myriad of corporate and licensee queries on any given day. Thom also is responsible for the distribution of the SortEnsure™ product line. Colleen Cova, financial controller, keeps a close eye on finances and overall business activity while Melissa Katsimpalis, corporate relations director, manages corporate communications and assorted issues.

The main stable is not only home of the XY Inc. equine breeding program, it houses the offices of Brad Wedell, farm manager; and Christy Douglass, equine manager. As a sun-up to sun-down team, Brad and Christy are in charge of the care and feeding of XY Inc.’s equine herd of 35 horses and the daily upkeep of the headquarters’ park-like grounds.

XY Inc. Introduces Full SortEnsure™ Product Line for Licensees

While a decade of attention has been paid to XY Inc. scientific advances, in the last two years, another advance has been brewing:

SortEnsure™, a roster of nine pre-packaged products, improves quality, efficiency and overall cost of making sperm-sorting media.

General Manager Thom Gilligan, working with Chata, a Fort Collins-based company that packages chemical components, led the development of the SortEnsure™ product line. The core product, SortEnsure™ Bovine Sheath Fluid, has been tested by many XY Inc. licensees, and it and several other SortEnsure™ products have been adopted and are in routine use by licensees in the U.S., Mexico and Europe.

In conjunction, FloClenz™, a sterilizing cleanser solution and system, can be used in routine cleaning of the SortEnsure™ sheath fluid and sample fluid lines. FloClenz™ is pre-packaged in bags to further reduce chances of unwanted contamination.

A run down of the major advantages of using SortEnsure™ products include:

1. Highest water quality – All SortEnsure™ products are made with the highest quality water recognized in the U.S. The water is virtually free of impurities, which is critical to health of sperm.

2. Purity of chemicals – All SortEnsure™ products are made with high-quality chemicals at reasonable prices.

3. Reliability in formulation – SortEnsure™ Bovine Sheath Fluid is produced by qualified chemists who work within the rigorous Quality Control/Quality Assurance system that supports cGMP production demands of the pharmaceutical industry.

4. Long shelf life – SortEnsure™ products have a minimum shelf life of six months.

5. Minimal waste – SortEnsure™ products may be held for downtime periods, so there is less chance of unneeded waste.
Audubon Center for Research of Endangered Species is globally recognized for its wildlife conservation-directed research, which focuses on use of state-of-the-art assisted-reproductive technologies such as cryopreservation of sperm and embryos; artificial insemination; in vitro fertilization; and embryo transfer.

"Audubon Nature Institute recognizes the importance of this type of conservation work to future generations and is committed to making this success a reality," said Ron Forman, president and CEO of Audubon Nature Institute.

Throughout July and early August, XY Inc. sorted several samples of fresh domestic cat sperm ejaculates, which had been collected and express-shipped by the ACRES research team.

Once the sperm were sorted, they were express-shipped back to ACRES where Dr. C. Earle Pope, senior scientist and ACRES research team leader for this project, and others produced embryos, using sexed sperm in a petrie dish. Two days later IVF embryos were transferred to recipient female cats and after a 62-day gestation, the kittens were born, marking the success of this pioneering research.

“Combining the ACRES team with XY Inc.’s 10 years of globally recognized advancements in sex selection in animals can only benefit endangered felines,” said Dr. Elizabeth Crichton, XY Inc. reproductive physiologist. Dr. Crichton focuses her research efforts in the study of sperm and their preservation in wildlife and exotic mammalian species.

Dr. Pope, a reproductive physiologist world renowned for his work with the advancement of assisted-reproductive technologies and their application to wildlife, took a lead in the sex-selection work with XY Inc. He is an expert in intra- and inter-species embryo transfer of in vitro derived embryos.

“We couldn’t be happier with these births,” said XY Inc. CEO Mervyn Jacobson. “Sex selection is critically important in the race against extinction of endangered exotic feline populations.”

Concluded Dr. Pope, “Our ability to determine the birth of female felines in captivity will help advance the work of animal preservationists trying to increase the numbers of endangered felines in the wild.”

“The world’s fastest land animal, the sleek and long-legged cheetah, Acinonyx jubatus, is losing its race for survival. Once a common animal found on five continents, the cheetah is now an endangered species. (Photo courtesy of Audubon Zoo, New Orleans, USA)
Throughout 2005-06, many XY Inc. licensees signed or became more active under XY Inc. commercial licenses. These include: Dansire, Denmark; Boviteq (Semex), Canada; and Live Stock Improvement Association of Japan and Hokkaido Genetics, both in Japan. XY Inc. also has signed agreements with researchers and entrepreneurs in Chile, China, Estonia, South Korea and Russia.

- **Dansire International.** Located in Randers, Denmark, Dansire, a leading Scandinavian supplier that provides genetics to Denmark, Sweden and Finland, signed a commercial license with XY Inc. to make and sell sexed dairy sperm. Dansire has established a state-of-the-art laboratory to house sperm sorters and currently is conducting field trials.

- **Genetics Hokkaido, Hokkaido, Japan.** Genetics Hokkaido, signed a commercial license in September 2005 and has begun field trials.

- **Goyaike S.A.** Longtime licensee, Goyaike, in Argentina, was approved to begin sales of sexed cattle sperm in Brazil. XY Inc. also approved Goyaike to commence sales of equine sexed sperm in Argentina.

- **IND Lifetech.** Vancouver, Canada, was approved in 2005 to begin selling sexed IVF embryos and sexed sperm for use in artificial insemination in China. In September 2006, IND was approved to begin international sales of sexed sperm for AI.

- **Inguran.** XY Inc.’s first US licensee operates sperm-sorting facilities in Texas, Brazil, Wisconsin and Ohio.

- **L'Alliance Boviteq (Semex).** In September 2006, XY Inc. approved Boviteq to commence commercial sales of sexed cattle sperm in Canada and the US.

**Expanding Interest.** In addition to the express strong interest in securing signed Holland, New Zealand, and the Ukraine.
Livestock Improvement Association of Japan.
Established in 1965, LIAJ, one of Japan’s top commercial cattle-breeding enterprises, has begun commercial sales of sexed embryos and sperm in 2006 under a license granted by XY Inc.

Neimenggu Sexing Art LTD.
A commercial licensee of XY Inc., Neimenggu Sexing Art LTD., located in Hu Hot, China, has teamed with China’s largest dairy, Mengniu, to sell sexed dairy sperm.

current licensing agreements, XY Inc. is negotiating with 15 parties throughout the world that agreements. At the moment, discussions are ongoing in Australia, Germany, India, Italy, Hawaii,
Some XY Inc. Achievements in 2005

- Geoffrey Gardiner Foundation Provides Major Grant to Optimize Sperm Sorting in Australia
A year later, joint research to improve sperm sorting in the Australian cattle has picked up its pace, thanks to the Geoffrey Gardiner Dairy Foundation, which in late 2005 provided a grant totaling $2.2 million.

The grant was made jointly to Total Livestock Genetics and the University of Sydney, where XY Inc. research associates are working with improved sexing techniques. Formed in 1989, TLG has traditionally offered bovine semen and embryo services.

The foundation was established in 2001 to increase the international competitiveness of the Victoria, Australia, dairy industry. Victoria is responsible for 63 percent of Australia’s milk production, 75 percent of Australia’s manufactured dairy products and 85 percent of Australia’s dairy exports, according to Australia’s Minister for Agriculture Bob Cameron.

- XY Inc. Entered New Research Collaboration with Colorado State University
In 2005, Colorado State University Professor Jim Graham, who also serves as XY Inc.’s scientific advisor, initiated an XY Inc.-sponsored research program to study cryopreservation of sex-sorted stallion sperm. Mindy Myers, an XY Inc. employee, who has entered a master’s program at Colorado State to study equine reproductive techniques, assisted Dr. Graham.

In 2006, their work has focused on such areas as different freezing rates and different diluents of stallion sperm; protein additives and yolk replacement related to medium preparation; external cryoprotectants; and longevity of sorted stallion sperm.

- CEO Jacobson Among Elite Entrepreneurs
XY Inc. CEO Mervyn Jacobson was one of 24 individuals from several different industries chosen as finalists for the 2005 Rocky Mountain Entrepreneur of the Year Award.

The finalists were selected by an independent panel of judges composed of leading CEOs and academic administrators throughout the American West and honored at a black-tie event in Denver, Colo., in June 2005.

Now in its 20th year, the Ernst & Young Entrepreneur of the Year is the world’s most prestigious business award. Recognized globally, the award honors the most outstanding entrepreneurs who inspire others with their vision, leadership and achievement.

Dr. Mervyn Jacobson (left) was chosen as a finalist for the 2005 Rocky Mountain Entrepreneur of the Year Award.