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01 SABER™ Delivery System (Injectable)
02 TRANSDUR™ Transdermal Technology
03 ORADUR™ Sustained Release Oral Gel-cap
04 DUROS® Implant System
05 DURIN™ Biodegradable Implant




(Post Operative Pain Relief Depot) SABER-Bupivacaine 01
(7-Day Pain Patch) TRANSDUR-Sufentanil 02
(Remoxy™) ORADUR-Oxycodone 03
(Sufentanil) CHRONOGESIC® Pain Therapy System 04
DURIN-Leuprolide 05

- 01 Liquid Injectable
- 02 Transdermal Patch
- 03 Oral Gelcap
- 04 Subcutaneous Implant (long-term)
- 05 Subcutaneous Implant (biodegradable)

FIVE NOVEL
DELIVERY SYSTEMS
FOR FDA APPROVED
THERAPIES

- Post-operative Pain 01
- Chronic Pain 02
- Chronic Pain 03
- Chronic Pain 04
- Alzheimer's Disease 05

FIVE
INDICATIONS
WITH LARGE
UNMEET NEEDS



05 Specialty
— pharmaceutical
systems.
Enabling
biotechnology.

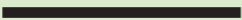
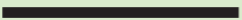
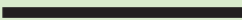
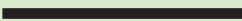
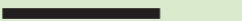
—
MANY SOURCES
OF POTENTIAL
REVENUE
AND PARTNERS



Better treatments 05
— for chronic, —
debilitating disease.
Improving
quality of life.

—
ONE
LONG-TERM
MISSION

Clinical Pipeline

| | | |
|---|--|--|
| <p>01</p> <p>PRODUCT: Post Operative Pain Depot</p> | <p>TECHNOLOGY: SABER Delivery System (injectable)</p> <p>INDICATION: Post-Operative Pain</p> | <p>PARTNER: DURECT Corporation</p> <p>PRE P1 P2 P3 NDA</p>  |
| <p>02</p> <p>PRODUCT: Transdermal Sufentanil Patch</p> | <p>TECHNOLOGY: Transdermal Technology</p> <p>INDICATION: Chronic Pain</p> | <p>PARTNER: Endo Pharmaceuticals, Inc.</p> <p>PRE P1 P2 P3 NDA</p>  |
| <p>03</p> <p>PRODUCT: Remoxy™</p> | <p>TECHNOLOGY: ORADUR (sustained release oral gel-cap)</p> <p>INDICATION: Chronic Pain</p> | <p>PARTNER: Pain Therapeutics, Inc.</p> <p>PRE P1 P2 P3 NDA</p>  |
| <p>04</p> <p>PRODUCT: CHRONOGESIC®</p> | <p>TECHNOLOGY: DUROS Implant Technology</p> <p>INDICATION: Chronic Pain</p> | <p>PARTNER: Endo Pharmaceuticals, Inc.</p> <p>PRE P1 P2 P3 NDA</p>  |
| <p>05</p> <p>PRODUCT: DURIN™ Leuprolide</p> | <p>TECHNOLOGY: DURIN Biodegradable Implant</p> <p>INDICATION: Alzheimer's Disease</p> | <p>PARTNER: Voyager Pharmaceuticals, Inc.</p> <p>PRE P1 P2 P3 NDA</p>  |

Corporate Highlights

| | MONTH | YEAR |
|---|-------|------|
| <p>March 14, 2005 - DURECT Corporation And Endo Pharmaceuticals Sign Agreement to Develop And Commercialize DURECT's Seven-Day Transdermal Pain Patch</p> | 03 | 05 |
| <p>February 16, 2005 - DURECT Initiates Phase II Program for Its Sufentanil Patch Product</p> | 02 | 05 |
| <p>February 10, 2005 - DURECT Completes Dosing of the Phase I Pharmacokinetic Study for Its Sufentanil Patch Product and of the First Cohort of the Phase II Study for Its Post-Operative Pain Relief Depot</p> | 02 | 05 |
| <p>January 28, 2005 - DURECT Corporation Announces Completion of Clinical Trial Enrollment for DURIN™-Based Leuprolide Product Candidate</p> | 01 | 05 |
| <p>December 23, 2004 - DURECT Corporation Announces Initiation of Phase III Studies for Remoxy, a Novel Oral Pain Medication using the ORADUR™ Gel-Cap</p> | 12 | 04 |
| <p>December 20, 2004 - DURECT and Voyager Pharmaceutical Announce the Acceptance of DURIN™ Investigational New Drug Application and Clinical Protocol by the FDA for the Treatment of Alzheimer's Disease</p> | 12 | 04 |
| <p>October 25, 2004 - DURECT Initiates Phase II Clinical Program for Post-Operative Pain Relief Depot</p> | 10 | 04 |
| <p>October 22, 2004 - DURECT Initiates Phase I Trial for Its Proprietary Transdermal Sufentanil Patch</p> | 10 | 04 |
| <p>July 6, 2004 - DURECT Announces Positive Clinical Results with its ORADUR™ Sustained Release Oral Gel-cap Technology</p> | 07 | 04 |
| <p>June 21, 2004 - DURECT Corporation and NeuroSystem Corporation Announce Exclusive Agreement to Develop Treatments for Certain Inner Ear Disorders Including Tinnitus</p> | 06 | 04 |

TO OUR SHAREHOLDERS

We are delighted to report that 2004 was the year where we saw the transformation of DURECT from a company that was focused on a single product candidate, CHRONOGESIC[®], to a company with a diversified pipeline of five product candidates in advanced development, namely, the SABER[™]-Bupivacaine injectable depot, TRANSDUR[™]-Sufentanil Patch, ORADUR[™] Oxycodone (Remoxy[™]), CHRONOGESIC[®] Implant and DURIN[™]-Leuprolide.

The success that we have achieved is based on the foundation we laid since the founding of DURECT in 1998, and on which we have continued to build such that, to date we have established a broad base of proprietary injectable, oral, transdermal and implantable technologies suitable for the treatment of chronic debilitating diseases and the enabling of biotech technology products. This broad technology base has allowed us to diversify our product portfolio and minimize our development and financial risk by establishing partnerships. In addition, the strength of our technology and product portfolio allowed us to execute on late-stage development agreements and maintain commercial rights on select products to further our goal of developing into a specialty pharmaceutical company with sales and marketing capabilities to drive greater shareholder value.

The highlights of the year include:

- On the strength of positive Phase I data, our SABER-Bupivacaine product candidate entered Phase II clinical testing at the end of 2004. This product candidate is intended to be administered around a surgical site after surgery to provide up to 72 hours or more of regional pain relief and is based on our patented SABER delivery system. We believe this product could potentially reduce hospital stays and the amount of traditional post-surgical pain medications needed by patients, as well as the side effects that result from the use of concomitant opioid medications. Although there has been significant interest from potential commercialization partners for this product candidate, we are evaluating retaining commercialization rights for this product candidate to further our goal of developing into a specialty pharmaceutical company.
- Based on the infrastructure and the clinical and delivery experience that we have developed on sufentanil through our CHRONOGESIC program, we established a transdermal program to develop a product that also enhances our return on our sufentanil investment. Our TRANSDUR Sufentanil patch for the treatment of chronic pain is designed for a dosing period of one week and is about one fifth the size of currently marketed opioid patches. This program has moved very rapidly, from initial

concept about eighteen months ago to the initiation of Phase II studies this year. As a result of our progress, we established a strong commercialization partnership with Endo Pharmaceuticals on this product candidate in March 2005 for the U.S. and Canadian markets under which we retain co-promotion rights, as well as all commercial rights for non-North American territories, to support our transition into a specialty pharmaceutical company.

- Remoxy (ORADUR-Oxycodone), a product candidate utilizing ORADUR, our proprietary oral sustained release gel cap technology under development in collaboration with Pain Therapeutics advanced into Phase III clinical testing at the end of 2004.
- DURIN Leuprolide for the treatment of Alzheimer's disease, under development in collaboration with the private company Voyager Pharmaceuticals advanced into clinical testing. In 2004, Voyager filed an IND and initiated Phase I testing on this product candidate while simultaneously conducting Phase II proof-of-concept studies.
- In 2004, we reported that our CHRONOGESIC program for the development of a product candidate to deliver sufentanil from the DUROS implant for the treatment of chronic pain, has been delayed after we continued to see a small fraction of systems experience a pre-mature shut down prior to end of the intended drug delivery period in animal testing. We continue to work on redesigning the system to address this issue.

In summary, DURECT met all of its corporate goals in 2004 for four of its five programs in development. In addition to advancing our product pipeline, we achieved regulatory milestones with the acceptance of two INDs for product candidates utilizing our technologies and continued to build on our strong patent position covering our technologies. We have a strong position in intangible assets such as "know-how" and other intellectual property to protect our products. Each of our products, both licensed and proprietary, possess key attributes critical to becoming a successful product in the large and growing markets they address. There is tremendous enthusiasm and optimism at DURECT because of the quality of the products we are developing and their increasing stage of maturity.

On behalf of everyone at DURECT, we thank you for your continued support and look forward to the achievement of major milestones in 2005.

Sincerely,

James E. Brown, D.V.M. *President and Chief Executive Officer*

Felix Theeuwes, D.Sc *Chairman and Chief Scientific Officer*

Thomas A. Schreck *Chief Financial Officer*



SABER POST-OPERATIVE PAIN DEPOT

The SABER system is a patented controlled-release technology that can be formulated for systemic or local administration of active agents via the parenteral or oral route. We are researching and developing a variety of controlled-release products based on the SABER technology.

We believe that our SABER system can provide the basis for the development of a state-of-the-art biodegradable, controlled-release injectable. The SABER system uses a high-viscosity base component, such as sucrose acetate isobutyrate (SAIB), to provide controlled release of the drug. When the high viscosity SAIB is formulated with drug, a biocompatible diluent (solvent) and other additives, the resulting formulation is liquid enough to inject easily with standard syringes and needles. After injection of a SABER formulation, the system sets up in a viscous, matrix of the three components — SAIB, drug, and any additives. Depending on how it is formulated, the SABER system can successfully deliver therapeutic levels of a wide spectrum of drugs from 1 day to 3 months from a single injection. The SABER Technology is the basis of our injectable post-operative pain relief depot product candidate currently under Phase II clinical testing.

Our SABER-Bupivacaine product candidate is a long-acting local anesthetic being developed for the treatment of post surgical pain and is intended to deliver from a single injection uninterrupted regional pain relief regional for up to 72 hours or more, which we believe coincides with the time period of the greatest need for post surgical pain control in most patients.

There are over 70 million combined inpatient and outpatient surgical procedures performed each year in the United States. We believe that SABER-Bupivacaine could be utilized in 40%-60% of these procedures (including abdominal, orthopedic, hernia, and many others types of procedures). Physicians that participated in DURECT's market research on this product indicated that SABER-Bupivacaine would represent a significant innovation over currently available postoperative pain relief therapies. Pain has been deemed by the WHO as the "5th Vital Sign," and stated that pain is significantly under treated. SABER-Bupivacaine may offer a significant improvement in post-operative analgesia. It can also potentially reduce opioid consumption, the amount of time hospital staffs spend managing post surgical pain and the duration of hospital stays.



"Working with visionary scientists and engineers is what I want and is the environment DURECT provides."

Eric Sheu *Principal Scientist*

TRANSDERMAL SUFENTANIL PATCH

Developing small, non-irritating and user-friendly products with excellent skin-adhesion are the main objectives for our TRANSDUR technology, which are major differentiating factors to patients and physicians that require a transdermally administered therapy.

Depending on the drug and its physiochemical properties, our TRANSDUR technology provides thin solid-state transdermal products that can deliver drugs, through the skin, at a controlled rate up to one week. TRANSDUR technology encompasses proprietary product components, which enable our scientists to expand the range of drugs that can be delivered transdermally. Transdermal products based on TRANSDUR technology can improve convenience and compliance as well as cost-effectiveness, and provide highly reliable therapy to patients and health care providers. Our TRANSDUR technology is the basis for our transdermal sufentanil patch product candidate under collaboration in the U.S. and Canadian markets with Endo Pharmaceuticals, Inc.

Our proprietary TRANSDUR-Sufentanil patch is a product under development for the treatment of moderate to severe chronic pain for once a week administration. Our sufentanil patch is a matrix-style transdermal patch that incorporates sufentanil, an opioid analgesic that is currently FDA approved for use in hospitals and the active agent in our CHRONOGESIC® product under development, to provide extended chronic pain relief for up to seven days, as compared to currently available three-day opioid patches. Also, the small size of the sufentanil patch, approximately one-fifth the size of other currently available opioid patches, may offer significant patient benefits. The product is currently undergoing Phase II clinical testing.

Physicians that participated in DURECT's market research on TRANSDUR-Sufentanil patch indicated that this product would represent a significant innovation over currently available transdermal pain relief therapies. Some of the expected product benefits include improved convenience and patient compliance, reduced skin irritation, cosmetic and quality of life improvements, improved patch adhesion and easier for high dose patients who require multiple transdermal patches.

"It is a rare opportunity to be part of a team that will greatly improve healthcare through its own talent, innovations, and hard work."

John Culwell *Senior Director of Project Management*



REMOXY

Our ORADUR technology is a sustained release oral gel-cap containing the drug in the SABER matrix to deliver over a 12 to 24 hour period. The ORADUR gel-cap may also be resistant to drug abuse (e.g., by crushing or alcohol or water extraction) as compared to other controlled release dosage forms on the market today. ORADUR-based products can be manufactured by a simple capsule filling process by conventional methods making them readily scalable. These properties have the potential to make ORADUR-based products an attractive option for pharmaceutical companies that seek to develop abuse resistant sustained release oral products.

Our ORADUR Technology is the basis of Remoxy, a novel long-acting oral formulation of the opioid oxycodone, and is targeted to decrease the potential for oxycodone abuse. Remoxy is a twice daily controlled release formulation that is intended to match the performance of Oxycontin®, but with enhanced abuse deterrence properties. Remoxy is developed under a joint development and commercialization agreement between DURECT and Pain Therapeutics, Inc. The product is currently under Phase III clinical testing by Pain Therapeutics, Inc.

Worldwide sales of Oxycontin, the leading sustained release formulation of oxycodone, exceeded \$2 billion in 2004. Diversion and misuse are a significant issue in the sale and distribution of strong opioids such as oxycodone. Abusers can easily extract the full dose from currently marketed time-release opioid preparations and administer the dose as a bolus (e.g. resulting in an immediate and large spike in opioid blood levels). This provides abusers with a fast and powerful morphine-like high. We believe that the ORADUR technology offers a significant advantage over other controlled release technologies as it is more difficult to misuse.



“Our focus at DURECT for the ORADUR technology is to demonstrate it’s capacity to mitigate the abuse potential of medicine, with Remoxy as a prime example.”

Wendy Chao *Director of Formulation Development*

CHRONOGESIC

DUROS® implant technology is coupled with proprietary drug delivery catheter and drug formulation technology. DURECT licensed the DUROS® technology for selected fields from ALZA Corporation in 1998. ALZA's Viadur® (leuprolide acetate implant) is the first approved product to be administered via the DUROS® System. The Food and Drug Administration approved the product in March 2000 as a palliative treatment for prostate cancer.

The DUROS system can be used for therapies requiring systemic or site-specific administration of a drug. To deliver drugs systemically, the DUROS system is placed just under the skin, for example in the upper arm, in an outpatient procedure that is completed in just a few minutes using local anesthetic. Removal or replacement of the product is also a simple, quick procedure completed in the doctor's office.

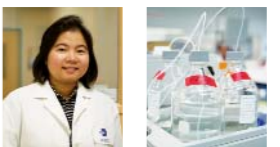
To deliver a drug to a specific site, DURECT is developing proprietary miniaturized catheter technology that can be attached to the DUROS system to direct the flow of a drug to the target organ, tissue or synthetic medical structure, such as a graft. Site-specific delivery enables a therapeutic concentration of a drug to be administered to the desired target without exposing the entire body to a similar dose. The precision, size and performance of the DUROS system will allow for continuous site-specific delivery to a variety of precise locations within the body. The DUROS system is the basis of our CHRONOGESIC® product candidate under development in collaboration with Endo in the U.S. and Canada.

The CHRONOGESIC (sufentanil) Pain Therapy System is a subcutaneous implant that is intended to continuously deliver sufentanil, an opioid medication, for an extended duration. This product under development is intended to treat chronic pain. Sufentanil is an FDA approved opioid that is currently used as an in-hospital anesthetic. CHRONOGESIC is intended for stable, opioid responsive chronic pain patients of malignant and non-malignant origin. Since the product is fully implanted under the skin, this product can allow for greater physician control over administering clinically necessary opioid therapy to chronic pain patients with potentially less risk of misuse, abuse and diversion than traditional pills or patches.

Chronic pain, defined as pain that lasts 6 months or longer, affects as many as one in eight people worldwide (34 million Americans annually). The market for strong opioids in the treatment of pain has been estimated to exceed \$4 billion annually.

“DURECT management’s guidance and support allows me, as part of the Research and Development team, to cultivate and explore creative ideas pertaining to the Chronogesic Pain Therapy System.”

Reggie Ordonio *Senior Research and Development Technician*



DURIN

Our DURIN™ technology is a proprietary biodegradable implant that enables parenteral delivery of drugs for long-term delivery of active ingredients, from several weeks to six months or more using our Lactel® brand polymers and co-polymers of lactic and glycolic acid. The DURIN technology can deliver a wide variety of drugs including hydrophobic and hydrophilic compounds, as well as small and large molecule compounds. Our proprietary implant design allows for a variety of possible delivery profiles including first order, zero-order, delayed or biphasic drug release. Because DURIN implants are biodegradable, at the end of its delivery life, the body absorbs what remains of the DURIN implant.

DURECT is researching and developing products based on the DURIN technology for a variety of chronic disease applications. The DURIN technology is the basis of DURIN-Leuprolide, our product candidate for the treatment of Alzheimer's disease that is currently in Phase I/II clinical development program by Voyager Pharmaceutical Inc.

DURIN-Leuprolide is a product candidate under development for the treatment of Alzheimer's disease that uses our proprietary DURIN technology to provide sustained release of the peptide leuprolide acetate and is based on Voyager's Pharmaceuticals' (partner) patented method of treatment of Alzheimer's disease.

Alzheimer's disease is a progressive, irreversible brain disorder with no known cause or cure. Symptoms of the disease include memory loss, confusion, impaired judgment, personality changes, disorientation, and loss of language skills. Alzheimer's disease is the most common form of irreversible dementia, eventually leading to fatalities. Approximately 100,000 patients die and 360,000 new cases of Alzheimer's disease are diagnosed each year. It is estimated that by 2050, 14 million individuals in the United States will have this disease. It is estimated that by 2020, 30 million people will be affected by this devastating disorder worldwide. The market potential for Alzheimer's disease treatments is estimated to be in excess of \$10 billion.



"DURECT's approach includes the combination of formulation and engineering for drug delivery systems, which are expected to have a significant impact on various therapeutic areas."

Sanjay Goskonda *Director of Formulation Development*

BUSINESS DEVELOPMENT / PARTNERING STRATEGY

Partnering with pharmaceutical and biotechnology firms is a key component of our business strategy. In some cases, we will partner at a very early stage by means of research collaborations, and in other cases we will develop compounds on our own and commence clinical trials before seeking a development and/or commercialization partners.

At DURECT, we understand the complexity and challenges pharmaceutical companies face in bringing new drugs to market. We also understand that risk is inherent throughout the development and approval process. And we believe we can help companies manage and minimize this risk through unique partnering relationships. In addition, our delivery platforms may help extend the proprietary positions of your drug franchises and enable new claims with novel dosage forms.

At DURECT, we offer a broad range of innovative drug delivery systems that are an essential element to any new controlled-release drug product. We offer sustained release technology platforms that provide delivery of your product from days to years based on your therapeutic and business needs. Many, but not all, of these technology options can be found here on our website. Our dedicated team of scientists and formulators offer additional expertise to custom-tailor drug delivery to our client's needs, whether parenteral, oral, transdermal, local or topical. It is this experience and expertise that accelerate the product development timelines, reduce development risk and increase the probability for a successful outcome.

Our vision for product development is to combine known drugs (both in terms of efficacy and side effect profile) with proven systems to get drugs quickly to market and lower development risk.



CORPORATE DIRECTORY AND INFORMATION

Executive Officers

Felix Theeuwes, D.Sc.
*Chairman,
Chief Scientific Officer
and Director*

James E. Brown, D.V.M.
*President,
Chief Executive Officer
and Director*

Thomas A. Schreck
*Chief Financial Officer
and Director*

Jean I. Liu
*Senior Vice President
and General Counsel*

Paula Mendenhall, Pharm D.
*Senior Vice President
of Operations*

Su IL Yum, Ph.D.
*Senior Vice President,
Engineering*

Tai Wah Chan, Ph.D.
*Vice President,
Pharmaceutical Research
and Development*

Steven C. Halladay, Ph.D.
*Vice President,
Clinical and Regulatory*

Jian Li
*Vice President,
Finance and
Corporate Controller*

Board of Directors

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*Chairman,
Chief Scientific Officer
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James E. Brown, D.V.M.
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Thomas A. Schreck
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Simon X. Benito
Director

Michael D. Casey
Director

David R. Hoffmann
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Armand P. Neukermans, Ph.D.
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Jon S. Saxe
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Corporate Secretary

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Annual Meeting

The company's annual meeting
of stockholders will be held at
9:00 A.M. local time June 22,
2005 at Company Headquarters

Independent Auditors

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Transfer Agent

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Tel: 781.575.3400

SEC Form 10-K

A copy of the Company's annual
report to the United States
Securities and Exchange
Commission on Form 10-K is
available without charge upon
written request to:

DURECT Corporation
Attn: Investor Relations
10240 Bubb Road
Cupertino, California 95014

Trademarks

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TRANSDUR™, CHRONOGESIC®,
MICRODUR™ and LACTEL®
are trademarks of DURECT
Corporation. Other referenced
trademarks belong to their
respective owners.

Corporate Profile

DURECT Corporation is an emerging specialty pharmaceutical company focused on the development of pharmaceutical systems based on its proprietary drug delivery platform technologies that treat chronic debilitating diseases and enable biotechnology products. These platform technologies include the SABER™ Delivery System (a patented and versatile depot injectable useful for protein and small molecule delivery), the ORADUR™ sustained release oral gel-cap technology (an oral sustained release technology with several potential abuse deterrent properties), the DURIN™ Biodegradable Implant (drug-loaded implant system), the TRANSDUR™ transdermal technology, the DUROS® System, (an osmotic implant technology licensed to us for specified fields from ALZA Corporation, a Johnson & Johnson Company) and the MICRODUR™ Biodegradable Microparticulates (microspheres injectable system). DURECT also collaborates with pharmaceutical companies to develop and commercialize proprietary and enhanced pharmaceutical products based on its technologies. DURECT has five disclosed on-going development programs of which four are in collaboration with pharmaceutical partners

The statements in this report regarding DURECT's partnered and proprietary products in development and product development plans are forward-looking statements involving risks and uncertainties that can cause actual results to differ materially from those in such forward-looking statements. Potential risks and uncertainties include, but are not limited to, DURECT's ability to complete the design, development, and manufacturing process development of its products, manufacture and commercialize its products, obtain product and manufacturing approvals from regulatory agencies, manage its growth and expenses, manage relationships with third parties, finance its activities and operations, as well as marketplace acceptance of DURECT's products. Further information regarding these and other risks is included in DURECT's Annual Report on Form 10-K for the fiscal year ended December 31, 2004 filed with the SEC on March 11, 2005, DURECT's Quarterly Report on Form 10-Q and other periodic reports filed with the SEC under the heading "Factors that may affect future results." © 2005 DURECT Corporation

concept and design: extralarge, a design studio (www.xlstudios.com)



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